Report

Comparison of pain, motion, and edema after modified radical mastectomy vs. local excision with axillary dissection and radiation

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Summary

Recent data suggest that prognosis is similar for women with primary breast cancer whether they receive modified radical mastectomy (MRM) or local excision and axillary dissection with radiation (XRT). The effects of either of these treatments on arm mobility, pain, or edema have not been compared. To assess the impact of MRM or XRT on mobility, pain, or edema, we evaluated patients treated in a prospective randomized trial designed to assess prognosis following MRM or XRT. All were provided a standardized physical therapy program including arm mobilization, shoulder strengthening, prevention and treatment of upper extremity edema, and education about arm function.

Patients were evaluated for chest wall pain, arm motion, muscle strength, and edema as determined by circumferential measurements at the wrist, forearm, and arm. Evaluations were performed preoperatively and at yearly anniversaries of their surgery. Women receiving XRT had more chest wall tenderness at 1 and 2 years after surgery than those receiving MRM ($p_1 < 0.0001$ and $p_2 = 0.0007$ respectively). Those receiving MRM were slower to reach their preoperative range of motion (ROM) ($p_2 = 0.043$). Incidence of muscle weakness was similar in both groups. The few patients with local recurrence of tumor had more upper extremity edema than those who did not recur ($p_1 = 0.085$) at 1 year and ($p_2 = 0.02$) at 2 years. In patients who did not develop local recurrence, those who had received XRT had greater but nonsignificant increases in upper extremity circumferential measures compared with those receiving MRM at any anniversary evaluation.

Patients receiving MRM and XRT are likely to have some differences in functional outcome. These differences may be important to individuals and be significant in helping them choose between MRM and XRT based upon individual functional needs.

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Figure 1. Randomization and treatment scheme

<table>
<thead>
<tr>
<th>Primary breast cancer (lesion &lt;5 cm) randomized</th>
<th>MRM*</th>
<th>Node−</th>
<th>Follow*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excisional biopsy + radiation + axillary dissection*</td>
<td>Node+</td>
<td>Adjuvant chemo*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Node−</td>
<td>Follow*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Node+</td>
<td>Adjuvant chemo*</td>
<td></td>
</tr>
</tbody>
</table>

*Tamoxifen given for all ER+, post-menopausal women after 1984.
*No stratification for lesions >4 cm, as done in some other trials.

Introduction

Surgical management of primary breast cancer has evolved as a result of the need to devise a treatment that confers long term survival benefits and local control of disease with the best cosmetic result. The natural history of surgical treatment has changed from the radical mastectomy [1], to the extended radical mastectomy [2], to the modified radical [3], and most recently to segmental mastectomy or excisional biopsy and radiation therapy with axillary lymph node dissection [4–5].

The implications of the recent prospective studies designed to study prognosis in the face of changing surgical procedures [4, 5] are that many women with primary breast cancer have a choice in the treatment of their cancer. Data support the conclusion that breast conservation surgery does not carry a different prognosis than more ‘radical’ surgeries; hence, decisions may be made for reasons other than prognosis. Some have suggested that psychological issues may be the deciding factor in making choices [6]. Others suggest that cosmetic and functional considerations need to be weighed as critical factors.

Few data are available comparing the impact of different procedures, thought to have similar prognoses, on functional outcome. Function in this context includes arm motion, strength, and swelling, as well as arm and chest wall tenderness to palpation.

This study compares the rehabilitation outcomes of women participating in a prospective randomized trial designed to compare the survival of patients with primary breast cancer treated with modified radical mastectomy (MRM) vs. excisional biopsy, axillary dissection, and radiation therapy (XRT).

Traditionally, patients undergoing treatment for breast cancer were referred for rehabilitation services only when a problem arose. These problems were loss of shoulder motion, shoulder girdle and arm pain, upper extremity edema, and loss of arm strength [7, 8]. Some notable exceptions are the preventive strategies employed by centers using stress reduction therapy [9] and the American Cancer Society’s Reach to Recovery programs, which are treatments universally available.

Prior work, previously reported, gave us an opportunity to develop a treatment and monitoring protocol for patients undergoing axillary dissection [10]. The standardized program consisted of pre-operative evaluation, a post-operative treatment phase (Table 1), an intermediate treatment phase, and a long-term problem intervention phase. This program provided comprehensive care with good functional outcome, and has become standard rehabilitation for patients undergoing axillary dissection at NIH. All patients treated for primary breast cancer received this rehabilitation program.

It is the intent of this manuscript to elaborate on the differences and similarities in functional outcome between two groups of patients with primary breast cancer – two groups who differed only in the definitive treatment of their primary breast cancer. It is hoped that this information may be useful in assisting women to make individual choices that uniquely suit their physical, psychosocial, and functional needs.
Materials and methods

All patients entered into a prospective, randomized trial comparing MRM with XRT as treatment for primary breast cancer were studied. The breast cancer management scheme is presented in Fig. 1. All patients were operated by one of three staff surgeons who performed level 3 node dissections and spared the pectoralis major. XRT included opposing tangential fields to the breast itself, which are designed to include the internal mammary nodes and matching supraclavicular field. The axilla was irradiated only if there was inadequate dissection or erosion through the capsule. Total rads delivered were between 4,680 and 5,000.

A total of 247 patients were randomly assigned treatment, of whom 237 (116 MRM, 121 XRT) were evaluated for analysis. These 237 patients represent all patients from this study who had data available on rehabilitative outcomes associated with treatment.

Each patient received a pre-operative musculoskeletal examination and was thereafter followed in the Department of Rehabilitation Medicine for treatment and periodic follow-up. The evaluation included a standard goniometric measure of range of motion (ROM) of the cervical spine and shoulders; manual muscle test of the muscles of the shoulder girdle and shoulders, including serratus anterior, latissimus dorsi, and pectoralis major; assessment of pain in the neck, arm, and trunk; and circumferential measures of both arms at ulnar styloid, olecranon, and 35 cm proximal to the ulnar styloid. Chest wall tenderness was assessed by examiner palpation at the mid clavicular line. A whine or utterance of pain by the patient indicated its presence. The appearance of the irradiated breast was recorded. These descriptors included the color of the irradiated tissue and its elasticity, and its symmetry when compared to the opposite breast.

The treatment provided was standardized. The ROM program and rate at which motion advanced is described in Table 1. Patients were permitted pain medications as prescribed by their physician. Heat, cold, massage, and transcutaneous nerve stimulators were used as needed to relieve pain and promote motion. Their use was based on clinical judgment by trained therapists. Patients were discharged to a home maintenance program after achieving at least 110° flexion, 90° abduction, and 55° external rotation of the shoulder. The use of an overhead pulley was recommended for all patients to assist in ROM.

Table 1. Post-operative ROM program

<table>
<thead>
<tr>
<th>Post-op day</th>
<th>Flexion</th>
<th>Abduction</th>
<th>Internal/external rotation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–2</td>
<td>40°</td>
<td>40°</td>
<td>To tolerance of pain</td>
</tr>
<tr>
<td>3</td>
<td>45°</td>
<td>45°</td>
<td>To tolerance of pain</td>
</tr>
<tr>
<td>4–6</td>
<td>45°–90°</td>
<td>45°</td>
<td>To tolerance of pain</td>
</tr>
<tr>
<td>7</td>
<td>To tolerance</td>
<td>To tolerance</td>
<td>To tolerance of pain</td>
</tr>
<tr>
<td>or drains removed</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Comparison of pain, motion, and edema

Analyses were performed comparing rehabilitative outcomes between patients receiving MRM and XRT. Data from evaluations which took place within six months of an anniversary were used at the corresponding annual point. The outcomes measured included: a) the time interval elapsed before reaching functional range of motion on the operated side; b) the time interval elapsed before reaching pre-operative ROM; c) the incidence of muscle weakness in the serratus anterior, pectoralis major, and latissimus dorsi; d) changes in hand, forearm, and arm circumference; e) the prevalence
Table 2. Days until ROM achieved

<table>
<thead>
<tr>
<th>Group (n)</th>
<th>Number of days (median; mean ± SE)</th>
<th>P-value***</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional ROM Group (n):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XRT (78)*</td>
<td>42.5; 66.0 ± 9.7</td>
<td>p = 0.55</td>
</tr>
<tr>
<td>MRM (87)</td>
<td>45.0; 77.6 ± 9.6</td>
<td></td>
</tr>
<tr>
<td>NO CHEMO (100)</td>
<td>42.5; 70.3 ± 8.7</td>
<td>p = 0.43</td>
</tr>
<tr>
<td>CHEMO (65)</td>
<td>48.0; 75.0 ± 11.1</td>
<td></td>
</tr>
<tr>
<td>Pre-operative ROM Group (n):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XRT (63)</td>
<td>93.0; 171.9 ± 24.1</td>
<td>p = 0.043**</td>
</tr>
<tr>
<td>MRM (65)</td>
<td>147.0; 194.8 ± 18.1</td>
<td></td>
</tr>
<tr>
<td>NO CHEMO (77)</td>
<td>120.0; 195.8 ± 20.8</td>
<td>p = 0.54</td>
</tr>
<tr>
<td>CHEMO (51)</td>
<td>117.0; 165.0 ± 20.7</td>
<td></td>
</tr>
</tbody>
</table>

*Numbers in parentheses refer to numbers of persons.
**Marginally significant, and suggestive, in light of multiple comparisons undertaken.
***As determined by the Wilcoxon rank survey procedure.

* of chest wall tenderness; f) change in ROM over the first year follow-up period.

Comparison between the conserved radiated breast and the unoperated breast is also presented, based upon observation, palpation, circumferential measurement, and assessment of skin elasticity using a calibrated syringe in mm gradations.

**Statistical analysis**

The Wilcoxon rank form was used to compare changes in range of motion versus baseline, the time interval elapsed before reaching either the functional range of motion or the preoperative range of motion, and the increase in edema between two groups (i.e. XRT vs. MRM, chemotherapy vs. no chemotherapy, and local failure vs. no local failure). Fisher’s exact test was used to compare the proportions of patients with chest wall tenderness according to primary treatment (XRT vs. MRM) or use of chemotherapy. The chi-square test was used to compare the distribution of edema between treatment groups. All p-values reported are two sided, and have not been corrected for the multiple comparisons made.

**Results**

There were 165 patients from whom we had preoperative and post-operative data about when functional range of motion was reached. Functional ROM (FROM) is at least 160° flexion, 145° abduction, and 80° of external and internal rotation. Seventy-eight had received XRT and 87 MRM. The mean number of days required to reach FROM was 66.0 in the XRT and 77.6 in the MRM group (p < 0.55). The receipt of chemotherapy did not prolong the time at which functional FROM was achieved (see Table 2).

Data are available for 128 patients for the time interval elapsed until preoperative ROM was met. Sixty-three had received XRT and 65 MRM. The average number of days elapsed before preopera-
tive ROM was 171.9 and 194.8 respectively ($p_2 = 0.043$). The receipt of chemotherapy did not delay return to pre-operative ROM (see Table 2).

We evaluated patients for changes in ROM over the first postoperative year. There is no significant loss in ROM over the first year in either flexion, abduction, or external or internal rotation. Data from patients receiving MRM or XRT were comparable.

The incidence of chest wall tenderness (Table 3) was significantly higher in patients receiving XRT than those receiving MRM ($p_2 < 0.0001$ at 1 year, $p_2 = 0.0007$ at 2 years). This was determined by palpation of the anterior chest wall in the mid-clavicular line. Chest wall tenderness persisted more than one year following completion of XRT. Chemotherapy did not influence this outcome. The numbers for evaluation are small and do not permit statistical analysis, but the percentage of patients who decreased their chest wall tenderness over the years is approximately 20% for patients with XRT and 10% for patients treated with MRM.

The serratus anterior muscle was most frequently found to be weak, followed by the pectoralis major and the latissimus dorsi. Muscle weakness was transient and returned to full strength within one year. The incidence of muscle weakness did not differ between the two treatment groups.

There were 10 in the XRT and 12 in the MRM group with serratus weakness, 8 in the XRT and 7 in the MRM group with pectoralis major weakness, and 5 in the XRT and 4 in MRM group with weak latissimus dorsi.

A total of 216 patients were evaluated for need of a compression sleeve during the first year post initial treatment. Twenty of 103 MRM were prescribed a compression sleeve and 23 of 113 XRT patients received a sleeve ($p_2 > 0.50$). In this study, a compression garment was routinely prescribed for any patient with a persistent increase in upper extremity circumferential measurement of >2cm.

There were 131 patients with both pre-operative and 1 year postoperative circumferential measurements of the upper extremity. Comparison of the frequency of edema is presented in Table 4. No significant differences were noted between the groups.

Patients who had local failure (recurrence of tumor at the chest wall only) had somewhat more arm swelling than those who did not locally recur. This difference showed a strong trend in the MRM

<table>
<thead>
<tr>
<th>Years since baseline</th>
<th>Local failure</th>
<th>Mastectomy increase* (N)</th>
<th>XRT increase* (N)</th>
<th>Overall increase* (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No</td>
<td>64, 1.76±0.23 ($P_2=0.078$)</td>
<td>55, 1.82±0.24 ($P_2=0.38$)</td>
<td>119, 1.79±0.16 ($P_2=0.85$)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>3, 3.43±0.54</td>
<td>9, 2.92±1.00</td>
<td>12, 3.05±0.75</td>
</tr>
<tr>
<td>2</td>
<td>No</td>
<td>28, 2.38±0.33 ($P_2=0.066$)</td>
<td>34, 2.58±0.37 ($P_2=0.20$)</td>
<td>62, 2.49±0.25</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>3, 5.90±1.82</td>
<td>4, 4.20±1.15</td>
<td>7, 4.93±0.99</td>
</tr>
</tbody>
</table>

* Average circumferential measurement in cm at largest anatomical segment.
group and in the group as a whole but was not significant in the group receiving XRT when looked at separately (Table 5). Data collected but not shown suggest that patients receiving XRT who do not have local recurrence have a slightly higher mean increase in circumferential measurements than do those with MRM, but these differences are not statistically significant.

Patients receiving XRT were evaluated for the cosmetic outcome of their treatment. At one year, data from 121 patients were available for evaluation. Twenty-two patients had some breast enlargement on the side receiving XRT. None of these breasts showed pitting edema. Two breasts were retracted and firm, creating an asymmetrical appearance for which patients chose to receive reduction mammoplasty on the contralateral side. Skin elasticity was reduced to <3 mm in six patients.

Discussion

Women with primary breast cancer treated with MRM and XRT demonstrate little difference in prognosis [1–3]. The results of a prospective study comparing these two groups, both of which received a standard program of post-operative rehabilitation, suggest that functional differences do exist between the two groups as a result of treatment for their primary breast cancer.

Return of function following treatment of breast cancer in which axillary dissection is performed is dependent upon several factors. These include the properly timed mobilization of the shoulder to assist the patient in achieving normal or pre-operative ROM, the instruction to the patient in use of antigravity pumping to prevent the development of edema, and the instruction of the patient in proper strengthening activities. All patients in this study received these interventions. Hence the differences are likely attributable to the difference in treatment for their primary breast cancer.

Functional outcomes that distinguished the two groups and reached statistical significance include frequency of chest wall pain, and length of time required to reach pre-operative arm ROM.

Chest wall tenderness was more frequent in the group receiving XRT. The explanation for this is not entirely clear, but is likely to be secondary to the influence of the XRT on the periostium of the ribs. Rib fractures were seen in the population that were not attributable to metastatic disease.

Patients receiving XRT were able to achieve their preoperative ROM faster than those receiving MRM. The clinical significance of this finding is minimal because it is the functional range that is the critical milestone to reach if usual activities are to be resumed. The XRT group may have reached FROM more quickly because while receiving six weeks of XRT at NIH they were also able to receive supervision and support for their therapy program. It is the policy of our Rehabilitation Department to supervise ROM during the entire radiation treatment course. The nature of the interventions, however, was no different from those for patients remote from NIH.

Another observation made during the study which distinguished the two groups, but did not reach statistical significance, was the greater increment in circumferential measurement of the arm at any anniversary evaluation in the group receiving XRT.

Circumferential measurements of the wrist, forearm, and arm were performed at yearly intervals in order to quantify change. Changes of less than 2 cm are considered normal variation. Changes of 2 to 4 cm are considered noteworthy. This change, were it to occur in the arm, might not be noticed by the physician and might not be experienced by the patient. An increase >4 cm is thought clinically significant, when it occurs in the forearm. A 6 cm increase in circumferential measure is clinically significant and often is associated with a functional impact. We treated edema >2 cm because our clinical experience has suggested that early treatment is beneficial to controlling or reversing the edema, but we acknowledge that increases in measurements of less than 4 cm are not thought to be clinically significant, and when in the arm are often not identified.

Local recurrence of tumor was associated with a significantly greater increase in upper extremity circumference. This was true for the group as a whole (ie. patients receiving XRT and MRM),
though the trend was strongest in the group receiving MRM. This difference may be secondary to the fact that local recurrence was a chest wall recurrence in the MRM group and was an in-breast recurrence in those receiving XRT. Chest wall recurrence may reflect more extensive disease than in-breast recurrence.

The cosmetic results of those receiving XRT were good and patients were generally pleased with the outcome. However, the chest wall tenderness was a clinically significant problem often requiring local treatment for pain relief and/or the use of non-steroidal anti-inflammatory medication. Several patients were unable to resume their previous activity of tennis, yardwork, or violin playing. Bothersome to these patients was the inability to sleep comfortably in the prone position or to hug someone without discomfort.

Anecdotally, individuals did report that they believed XRT was associated with fatigue and they were not 'back to pre-treatment' functioning until it was completed. This observation was not noted for those receiving MRM, who returned to their pre-treatment level of functioning more quickly.

Data from seventy-two patients were not obtained for analysis. Patients lived remote from the NIH, and if they missed an appointment it was difficult to call them back for a measurement. Since many of the follow-up visits were for data collection and measurements, rather than for treatment, patients may not have felt as compelled to return for these follow-up appointments. It is unlikely that this created a new bias given that the proportion of patients receiving MRM or XRT remained the same.

Based on the data presented, patients receiving MRM and XRT are likely to have some differences in functional outcome. These differences are chest wall tenderness and arm edema, which may be important to some individuals. These differences may thus be useful in helping patients choose between MRM and XRT. Information about pain, motion, edema, and return to functional status is important to patients and should be shared at the time decisions are made about initial treatment.

References