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ORIGINAL ARTICLE – BREAST ONCOLOGY

Implementing the Prospective Surveillance Model (PSM) of Rehabilitation for Breast Cancer Patients with 1-Year Postoperative Follow-up, a Prospective, Observational Study

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ABSTRACT

Background. The Prospective Surveillance Model (PSM) of rehabilitation for patients with breast cancer aims for early identification, treatment, and support of physical impairments postoperatively. The purpose of this study was to describe the incidence of impairments during the first postoperative year and the differences between the patients requiring rehabilitation intervention versus those not requiring intervention.

Methods. A total of 120 patients were enrolled. Impairment measures included: pain, range of motion, and self-reported measures of function using the Upper Extremity Functional Index (UEFI) and Quick Disability of the Arm, Shoulder and Hand (QuickDASH) questionnaires. These measures were performed at designated intervals during the first postoperative year. All patients received exercise and education, and patients with identified impairments underwent individualized rehabilitation intervention. Clinical factors associated with need for intervention were determined using univariate analysis.

Results. Thirty-six patients required rehabilitation intervention. There were no statistically significant differences between intervention and no-intervention groups for body mass index, breast surgery type, reconstruction type, or radiotherapy. Statistically significant differences were found between intervention and no-intervention groups in early postoperative UEFI, QuickDASH, pain scores, age, number of lymph nodes removed [9.3 (intervention) vs. 5.6 (no-intervention)], axillary surgery type, chemotherapy, and breast cancer stage.

Conclusions. Survivorship practitioners should have heightened awareness for rehabilitation intervention in patients with greater axillary surgery and burden of disease. Patients with more activity restriction and lower levels of function in the early postoperative period may benefit from rehabilitation intervention. Future studies should focus on implementing a screening tool to identify patients in need of rehabilitation referral.

Breast cancer is the most common cancer among women with relatively high overall survival rates. Because of this, it is important to improve the comprehensive care for breast cancer survivors. Breast cancer survivorship must address a multitude of issues for patients including surveillance for and treatment of morbidity associated with cancer treatment.

Upper extremity morbidity from breast and axillary surgery varies widely and includes lymphedema, range of motion restriction, axillary web syndrome, numbness, weakness, and pain. Of these, lymphedema is the most widely studied and clinically recognized. The reported incidence of lymphedema in the literature varies according to length of follow-up and treatment factors of the cohort

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and is reported to be as high as 49 % of breast cancer survivors who were followed for 20 years after modified radical mastectomy.[1]

The Prospective Surveillance Model (PSM) of rehabilitation in breast cancer serves as a proactive approach to address the morbidity of breast cancer treatment seen in oncology rehabilitation and breast cancer survivorship and is described in Fig. 1.[2] The goals of the PSM are for early identification, treatment, and support of physical impairments and to teach patients skills and behaviors to promote their own health. Appointments with physical rehabilitation providers are generally scheduled concomitantly with medical providers to facilitate an integrated, multidisciplinary management plan.

We report the first prospective observational study of the PSM in postoperative breast cancer patients. The purposes of this study were to describe the incidence of postoperative impairments and activity limitations over the course of the first postoperative year and to describe the differences between the patients who were identified as needing rehabilitation intervention and those who were not.

METHODS

Patients

This study was performed at Grady Memorial Hospital, a safety net hospital in Atlanta, Georgia. Study approval was obtained from the Institutional Review Board. Eligibility criteria included English-speaking patients with stage 0-III breast cancer who had not yet undergone surgery. All eligible patients presenting to the breast clinic were approached for study enrollment. Patients provided informed consent for enrollment and treatment.

All patients were provided with a patient navigator, were educated about lymphedema, and received an early postoperative exercise program to help promote their overall health regardless of impairment status. Patients were evaluated preoperatively, in the early postoperative period (designated as 2–4 weeks), and at 6 weeks, 3-, 6-, 9-, and 12-months after surgery. Patients were assessed for upper extremity limitations at each visit by subjective and objective means.

Self-reported measures of function were performed at each visit utilizing the Upper Extremity Functional Index (UEFI) and Quick Disabilities of the Arm, Shoulder and Hand (QuickDASH) questionnaires and patient-reported pain level on scale of 1–10.[3,4] The UEFI assesses upper extremity functional status according ability to perform 20 activities rated on a 5-point Likert scale with 0 indicating inability to perform the activity and 4 indicating no difficulty to perform the activity. The total score ranges from 0 to 80 with a higher score signifying a higher functional status. The QuickDASH consists of 11 items to measure physical function and symptoms of musculoskeletal disorders of the upper extremity. The items are rated on a 5-point Likert scale with 1 indicating no limitation and 5 indicating extreme limitation. The total score ranges from 0 to 100 with a lower score signifying a lower level of disability. Measures of impairment were performed at each visit by a physical therapist and included measurement of shoulder range of motion, arm volume, and assessment for axillary web syndrome.

Upper extremity impairments triggering individualized rehabilitation intervention were defined as changes in the following measures compared with preoperatively: lymphedema >3 %, increase in arm circumference >1 cm from baseline, shoulder range of motion decreased by 20°, presence of significant pain and/or activity limitation. Interventions were provided by a physical therapist and included manual therapy and soft tissue massage, treatment of cording, targeted home exercise, and/or lymphedema treatment. Lymphedema intervention was individualized and included detailed education, compression, scar massage, exercise, and/or manual lymphatic drainage.

Data Analysis

Means and standard deviations for continuous data and frequency counts or percentages for categorical data were used to describe the entire study population and the patient groups who were identified as needing rehabilitation intervention and those who were not. The Fisher exact test was applied to between group comparisons for categorical data and *t* tests for independent sample means or Wilcoxon rank-sum test for continuous data depending on whether the requisite assumptions were met for parametric tests. All statistical analyses were performed utilizing STATA 14.1 software (STATA Corp, College Station, TX). Results were considered to be statistically significant if $p < 0.05$.

RESULTS

Enrollment consisted of 120 patients with stage 0-III breast cancer, of which 110 underwent surgery and were eligible for study. Exclusion criteria for patients initially enrolled included metastatic disease on further workup, patient decision not to undergo surgery, or transfer of care to another institution. Of the surgical patients, 21 % (n = 23) had Stage 0 breast cancer, 37 % (n = 41) Stage I, 30 % (n = 33) Stage II, and 12 % (n = 13) Stage III breast cancer. Breast-conserving surgery was performed for approximately two-thirds of the patients (65 %, n = 71). Table 1 demonstrates patient distribution according to type of

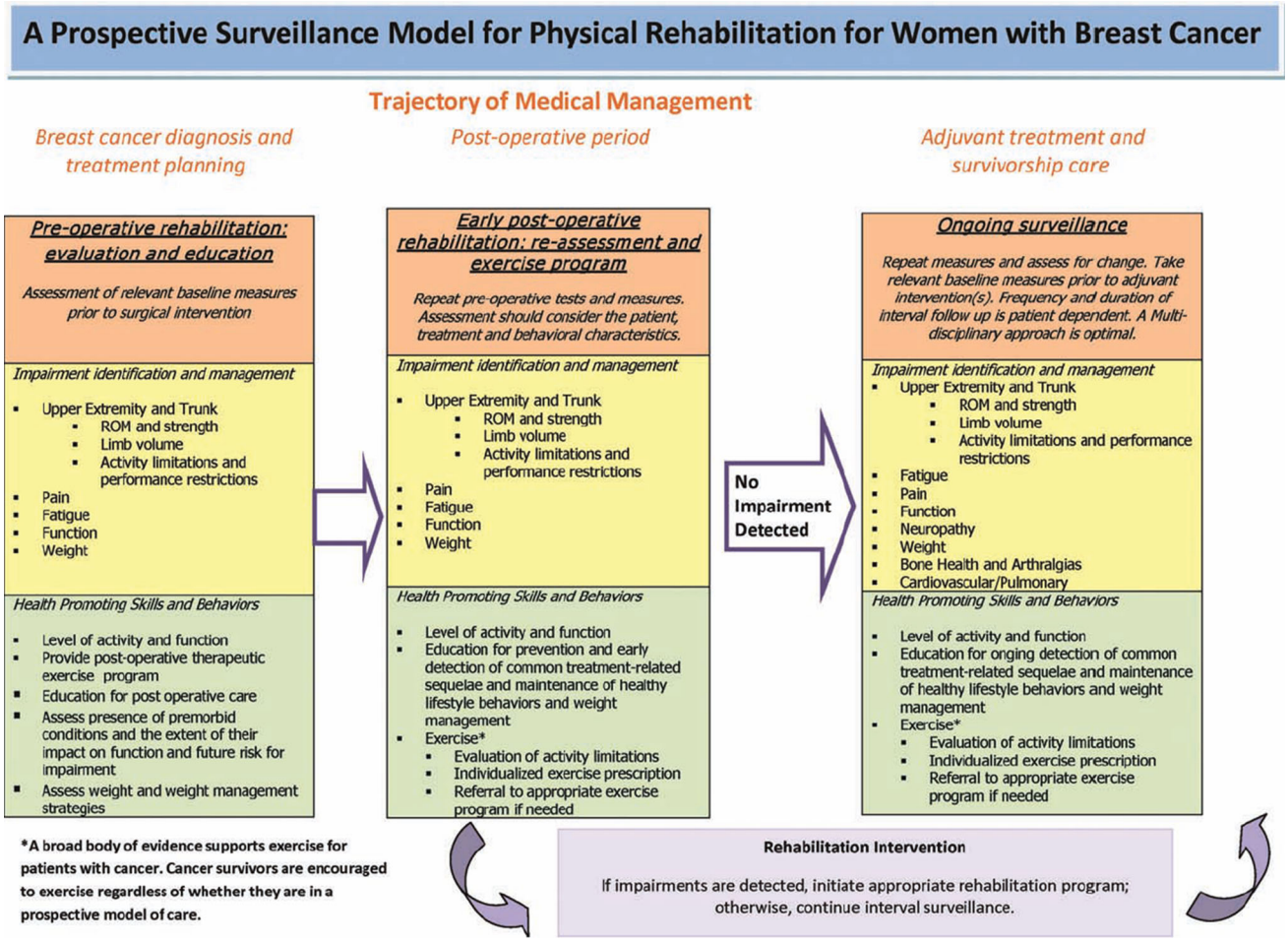

FIG. 1 Prospective Surveillance Model for Physical Rehabilitation for Women with Breast Cancer. Reprinted from "A Prospective Surveillance Model for Rehabilitation for Women With Breast Cancer" by N. L. Stout, et al. 2012, *Cancer*, 118(8 Suppl), p. 2193. Copyright 2012 by John Wiley and Sons. Reprinted with permission

TABLE 1 Patients according to type of axillary surgery

Type of axillary surgery	No. of patients (%)
No axillary surgery	18 (16)
Sentinel lymph node biopsy	60 (55)
Axillary lymph node dissection	32 (29)

axillary surgery. Sentinel lymph node biopsy was performed in just over half of patients, axillary lymph node dissection was performed in almost one-third of patients, and 16 % of patients did not have any axillary surgery. Nearly half of the patients (49 %, n = 54) had chemotherapy with 61 % (n = 31) of the chemotherapy recipients receiving it in the neoadjuvant setting. Two-thirds of patients (67 %, n = 74) underwent radiotherapy. Of those who had mastectomy (n = 39), 46 % had reconstruction with nearly even split between autologous flap reconstruction and tissue expander/implant-based reconstruction (n = 8 and n = 10, respectively).

One-third of all study patients met criteria for individualized rehabilitation intervention (33 %, n = 36) with some patients having multiple indications. Sixteen patients were identified with lymphedema: very mild <5 % (n = 3), mild 5–10 % (n = 9), moderate 11–15 % (n = 2), and severe >15 % (n = 2). The most common reason for intervention was for lymphedema, followed by decreased range of motion, and lastly for pain or axillary web syndrome.

The UEFI, QuickDASH, and pain scores were obtained at the designated follow-up appointments and found to have statistically significant prediction of need for intervention in the early postoperative period of 2–4 weeks as shown in Table 2 with the intervention group having lower functional index scores (36 vs. 52, p = 0.002), higher disability scores (50 vs. 37, p = 0.047), and higher pain levels (5 vs. 3, p = 0.028).

Comparisons of patient clinical and treatment factors among the intervention and no-intervention groups are shown in Table 3. There were no statistically significant

TABLE 2 Early postoperative patient self-assessment results according to intervention type

	Intervention (n = 36)	No intervention (n = 74)	p value
Mean Upper Extremity Function Index (UEFI)	36	52	0.002
Mean Quick Disabilities of the Arm Shoulder and Hand (QuickDASH) score	50	37	0.047
Mean pain score	5	3	0.028

TABLE 3 Patient characteristics and treatment factors according to intervention type

	Intervention (n = 36)	No intervention (n = 74)	p value
Mean number of lymph nodes removed	9.3	5.6	0.006
Chemotherapy (%)	24/36 (67)	30/74 (41)	0.01
Breast-conserving surgery (%)	20/36 (56)	51/73 (70)	0.154
Radiation (%)	27/36 (75)	47/73 (64)	0.264
Mean age (year)	55.1	59.2	0.049
Mean body mass index (kg/m^2)	34.5	32.6	0.277

differences in BMI, type of breast surgery, type of reconstructive surgery (p = 0.201), and radiotherapy between the two groups. There was no significant difference between shoulder flexion range of motion between the two groups.

The intervention group had significantly greater number of lymph nodes removed compared with the no-intervention group (9.3 vs. 5.6, p = 0.006), greater extent of axillary surgery as demonstrated by Fisher's exact test of axillary surgery type (p = 0.033), more patients who underwent chemotherapy (67 vs. 41 %, p = 0.01), greater overall burden of disease as demonstrated by the Mann–Whitney test on intervention according to breast cancer stage (p = 0.018; Table 4) and was younger than the no-intervention group (55.1 vs. 59.2 years, p = 0.049).

TABLE 4 Patient distribution and intervention according to breast cancer stage

Stage	Total number of patients	% Intervention
0	23	13
1	41	29
2	33	39
3	13	62

DISCUSSION

All of the patients in the study received education regarding treatment side effects, such as lymphedema, as well as an early range of motion exercise program. One-third of all study patients met preestablished criteria for individualized rehabilitation intervention (33 %, n = 36) with some patients having multiple indications. Sixteen patients were identified with lymphedema. It is of note that most of these patients were identified at the very mild and mild stage of lymphedema, one of the intents of the PSM. This suggests that the PSM for breast cancer patients was successful at identifying and treating lymphedema at an early stage.

Patients in the intervention group had lower levels of function at the early postoperative evaluation, as measured by the UEFI and QuickDASH and higher pain scores. Of interest is that there was no significant difference in flexion range of motion between the two groups, but there was a trend that the intervention group had lower range of motion. There was wide variability in range of motion measures that contributed to a lack of statistical finding.

Patients in the intervention group had significantly greater numbers of lymph nodes removed and greater extent of axillary surgery. Many studies have reported similar findings with increased risk of lymphedema with increase in number of lymph nodes removed, increased risk of lymphedema with greater extent of axillary surgery, decreased overall quality of life and arm function with greater extent of axillary surgery, and greater short and long-term morbidities with greater extent of axillary surgery.[5–15] Of note, there were patients in this study who had sentinel lymph node biopsy alone and still met criteria for intervention therefore rehabilitation referral decisions should not be based on absolute number of lymph nodes removed exclusively.

A significantly greater number of patients in the intervention group received chemotherapy, and there was a significantly higher average stage of breast cancer in this group. This association between greater burden of disease and disability also is noted in the literature and is likely

reflective of disability from the actual disease burden, the need for greater extent of surgery, and use of adjuvant therapies.[7] This may be due, in part, to musculoskeletal effects of treatment causing pain and decreased range of motion or fibrosis and alteration of lymphatic flow causing increased lymphedema. There is debate in the literature over effects of chemotherapy on development of lymphedema. In one study chemotherapy increased risk of lymphedema in breast cancer survivors who were subjectively assessed for lymphedema.[11] Other studies have examined specific chemotherapeutic agents especially taxanes, because taxane-based chemotherapy has been noted to cause fluid retention. In one study, patients undergoing adjuvant taxane-based chemotherapy were noted to have increased extracellular volume in all four extremities with persistence of elevated extracellular fluid volume in the arm ipsilateral to the breast cancer operation, whereas another study of a large, prospective cohort found those treated with docetaxel had mild extremity swelling but that it did not translate into subsequent lymphedema.[16,17]

The extent of axillary surgery in the intervention group was greater, but the extent of breast surgery (partial mastectomy versus mastectomy) was not significantly different between the two groups. Greater extent of breast surgery as a risk factor for lymphedema is reported in the literature with mastectomy patients having higher rates than partial mastectomy patients.[6,14] This may not be apparent in our study due to low rate of mastectomy compared with breast-conserving surgery. Additionally, a number of patients were lost to follow-up, which could have contributed to underreporting. Similarly, we did not see an association between the type of breast reconstruction and upper extremity impairment. This also could be attributed to the overall low number of patients having reconstruction. Effects of reconstruction on lymphedema incidence in the literature are encouraging with studies showing no adverse effects, protective effects of immediate reconstruction, and reduction of arm volume in patients with baseline lymphedema undergoing delayed reconstruction.[10,18–20]

In this study, there was no difference in the intervention group with respect to radiation. Data were not collected on radiation according to specific regimens, although each type of treatment may have different effects on the upper extremity. Some studies in the literature report effects according to specific regimens, with increased lymphedema noted in patients who underwent axillary radiation, nodal irradiation in addition to whole breast radiotherapy after breast-conserving surgery, and impaired shoulder mobility noted after axillary radiation.[7,21,22] Other studies report increased rates of lymphedema with radiation in general.[5,8,14] The AMAROS trial of axillary lymph node dissection versus axillary radiation for patients with positive sentinel node reported significantly lower lymphedema with axillary radiation than with axillary lymph node dissection.[23] We note a similar trend of axillary surgery contributing to a greater extent to upper extremity morbidity than radiation in our study population.

While there was a difference in age between the intervention and no-intervention groups, this small difference in age is not clinically significant. Most studies in the literature report that older age is a risk factor for lymphedema.[9,10,17]

There was no significant difference between the intervention group and no intervention groups with respect to BMI. This may be due to homogeneity in our subjects and lack of variability in data with 37 % of patients being overweight (BMI 25–30) and 55 % of patients being obese (BMI $>$ 30). Other studies have report obesity to be a risk factor for lymphedema and functional disability in general.[6,7,10,13,17] Weight gain over many years in the survivorship period also is associated with increased risk of lymphedema.[1]

There are several limitations to this study. This was a single-institution study conducted at a safety net hospital with a fairly homogeneous patient cohort. It is possible that these results may differ from those that would be seen in other health care systems or regions of the United States. This study was limited to 1-year of postoperative follow-up. This follow-up period was designated as a starting point for implementation of the Prospective Surveillance Model (PSM), but we recognize that breast cancer survivorship issues may arise beyond this period and last for longer timeframes. There was great initial interest in participation with approximately 90 % of eligible patients enrolling but ultimately just over 25 % of our cohort completed their 12-month follow-up visits.

Several reasons for patient dropout included: transportation issues, need to attend other therapies, return to work, and medical comorbidities. The PSM includes early education on postoperative exercise and lymphedema prevention. It could be that patients felt they had the necessary education and did not feel follow-up visits were needed if they were asymptomatic. Methods to increase patient follow-up could include increased phone call reminders, reminders sent by mail, parking reimbursement, transportation assistance, or a monetary incentive for follow-up.

Despite the limitations of the study, we believe this is the first study to implement the PSM for breast cancer patients. While it is resource intensive to assess patients prior to surgery and actively follow them for a period of time after treatment, we have identified clinical and treatment factors associated with patients who met our predetermined criteria for individualized rehabilitation intervention. In summary, they include: greater number of axillary lymph nodes removed and extent of axillary

surgery, chemotherapy, and higher breast cancer stage, as well as patient-reported functional assessments (UEFI, QuickDASH and pain score). Clinicians must have heightened awareness of upper extremity impairments in such patients with higher burden of disease, because there is a role for early referral and intervention to help decrease the morbidity of their breast cancer treatment. When considering lymphedema specifically, early patient education and detection is paramount as early intervention can interrupt lymphedema progression while in the latent and reversible stages. Future studies should focus on implementing a screening tool in surgeon practices or in survivorship clinics for the early identification of patients with functional limitations in need of rehabilitation intervention.

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