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TITLE: Modifiable Risk Factors for Lymphedema in Breast Cancer Survivors

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14. ABSTRACT Lymphedema of the arm is a consequence of breast cancer treatment that can result in substantial functional impairment and distress. In this study, women diagnosed with a first primary invasive breast cancer and treated with axillary lymph node dissection will be identified through a population-based cancer registry. The incidence and timing of arm edema will be assessed using physical measures (arm volume) and self-reported arm symptoms. To date, 423 women have been enrolled in the study; 218 women have participated in their first follow-up interview and 87 women in a second follow-up visit. A preliminary analysis, based on enrollment data, was presented at the DOD Era of Hope meeting in June, 2005. We found that increasing body mass was positively associated with the occurrence of arm swelling identified by self-report or by measured arm volume. Future analyses will assess changes in arm volume over time and relationships of arm swelling with treatment and lifestyle factors.					
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INTRODUCTION

Lymphedema of the arm is a common, yet dreaded consequence of breast cancer treatment that can result in substantial functional impairment and distress in affected women. Axillary surgery and radiation treatment are known risk factors for lymphedema. However, other potentially modifiable characteristics or behaviors that may influence risk of this condition have not yet been studied. In this study, we will assess whether modifiable factors, including body weight, physical activity, smoking, and breast reconstruction, influence risk of arm lymphedema among women treated for breast cancer. Women aged 21-74 years diagnosed with a first primary invasive breast cancer will be identified through a population-based cancer registry. Eligible women will be residents of King County, Washington. We aim to include approximately 500 women in the study cohort. Enrollment will be limited to women who have had axillary node dissection, as the occurrence of lymphedema is most common in these women. The incidence and timing of arm edema following breast cancer will be assessed using physical measures (arm volume) and self-report of symptoms, at regular intervals throughout the study. Each time they undergo arm measurement, women will complete questionnaires detailing and updating information on the exposures of interest and potential confounding factors. The study will be conducted over a 4-year period.

BODY

Research Accomplishments associated with tasks outlined in the Statement of Work are as follows:

Task 1. Develop Plan for Initial and Follow-up Interviews and Measurements, Months 1-3.

All of these tasks have been performed.

a. Final IRB approval will be obtained.

IRB approval has been obtained from the Fred Hutchinson Cancer Research Center and from the DOD.

b. Tracking system will be created to track patient contacts, recruitment, and interviews.
The tracking system for this study has been developed and is in use.

c. Cohort ascertainment through the CSS tumor registry will be initiated.

We are actively identifying potential study participants through the CSS tumor registry. Case-finding through the registry is updated every month.

d. Enrollment questionnaire will be developed, piloted and finalized.

The enrollment questionnaire has been developed, piloted and finalized. It is now in use.

e. Interviewer will be trained on study procedures, measurement, and interview administration.

Interviewer training on all study procedures, including measurement and interview administration, has been completed.

Task 2. Subject Recruitment and Initial Data Collection, Months 4-18

a. Potential study subjects will be contacted, and physician notification will be performed. These procedures are now ongoing. The first set of contacts with physicians and study subjects occurred after all Human Subjects approvals were obtained in May, 2003. As of mid-August, 2005, we had identified 644 eligible women. The status of the 644 women in the study is as follows:

Deceased, before contacted:	10
Physician notification/ response in process:	2
Physician refusal:	31
Physician notified, subject not yet contacted:	2
Study subject refusal:	99
Subjects contacted, not yet enrolled:	56
Subjects contacted, enrollment interview scheduled:	21
Subjects contacted, enrollment interview complete:	423

b. Participant enrollment interviews and initial measurements will be conducted.

We have completed 423 enrollment interviews, with an additional 21 interviews scheduled for the near future. We anticipate that enrollment interviews will be completed during the fall of 2005.

Subject recruitment and initial data collection is still ongoing. The number of subjects shown above reflects recruitment during the first 34 months of the study. As also reported last year, recruitment for the study has been slower than anticipated, due to the following: (1) The funding period for this study began on October 1, 2002. The DOD approval to involve human subjects in the research was received in April, 2003. Hence, we did not begin activities related to Task 2 until May, 2003 (month 8), and anticipated that the subject recruitment period would need to extend further into the study period than was originally planned. (2) The number of eligible women is also somewhat lower than expected, which we believe is due to the increasingly widespread use of sentinel biopsy of lymph nodes, with resultant decline in axillary dissection. (3) Some women are not identified by the cancer registry as eligible until a longer time period after diagnosis than we had originally expected. This can occur related either to reporting delays or to the use of neoadjuvant chemotherapy for some months prior to axillary dissection.

c. Follow-up questionnaires will be developed, piloted and finalized.

The first, second, and third follow-up questionnaires have been developed and finalized.

d. Data management and programming to create analytic data files for the enrollment questionnaire and arm measurement data will be performed.

These tasks have been completed, and preliminary data from the enrollment questionnaire and arm measures were presented at the DOD Era of Hope meeting in June, 2005. Additional variable creation for data analysis is ongoing.

Task 3. Follow-up Interviews and Data Collection, Months 10-45

a. Follow-up interviews and measurements will be conducted.

Follow-up interviews are ongoing. To date, 218 first follow-up interviews and 87 second follow-up interviews have been conducted. Seven women declined or were unable to participate in the first follow-up interview, and an additional 4 women declined the second follow-up interview. We anticipate that third follow-up interviews will commence in September, 2005. As also reported last year, we expect that the conduct of follow-up interviews will extend several months beyond month 45, into a planned no-cost extension, due to delays in study enrollment as described above under Task 2.

b. Data management and programming to create analytic data files from the follow-up questionnaires and repeat arm measurement databases will be performed.

These tasks will be initiated later this year, consistent with the delayed study enrollment (e.g., month 40 and beyond).

c. Identification of women with lymphedema by arm volume measures, and comparison with self-report.

These tasks will be conducted during the later months of the study (e.g., month 40 and beyond), using the follow-up questionnaires and arm measures. Preliminary identification of lymphedema using arm measures and self-report at the baseline interview was performed for a preliminary analysis reported at the DOD Era of Hope meeting in June, 2005.

Task 4. Data Analysis and Report Writing, Months 37-48.

These tasks will be delayed and conducted during a planned no-cost extension of the project, reflecting the delay experienced in initiating participant enrollment.

KEY RESEARCH ACCOMPLISHMENTS

- 423 women enrolled in the study to date.
- First follow-up interviews conducted on 218 women.
- Second follow-up interviews conducted on 87 women.
- Preliminary data analysis conducted and reported at the DOD Era of Hope meeting in June, 2005.

REPORTABLE OUTCOMES

Preliminary results were reported as a poster presentation and an oral presentation at the DOD Era of Hope Meeting in June 2005 (see abstract in Appendix).

CONCLUSIONS

In this early phase of the study, there are no completed research results on which to base conclusions. Some preliminary findings of the study were reported at the DOD Era of Hope Meeting in June, 2005. Please see attached abstract for summary.

REFERENCES

None

APPENDICES

Abstract presented at the DOD Era of Hope meeting is attached.

RISK FACTORS FOR LYMPHEDEMA IN BREAST CANCER SURVIVORS

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Lymphedema of the arm is a common, yet dreaded consequence of breast cancer treatment that can result in substantial functional impairment and distress. While axillary surgery and radiation treatment are known risk factors for lymphedema, few other characteristics that may influence risk have been studied. Through this research, we will assess whether modifiable factors, including body weight, physical activity, smoking, and breast reconstruction, influence risk of arm lymphedema.

We are conducting a prospective study in a cohort of women aged 21-74 years diagnosed with a first primary invasive breast cancer from October 2002- July 2004. Eligible women have undergone axillary dissection as part of their cancer treatment, and are identified through a population-based cancer registry in Washington State. The occurrence of lymphedema is assessed using physical measures and self-report at regular intervals throughout this four-year study. Arm circumference is measured at 1.5-inch intervals from hand to axilla, and these measures are converted to arm volume. Each time they undergo arm measurement, women also complete questionnaires detailing and updating information on the exposures of interest and potential confounding factors.

Results presented here are based on the baseline questionnaires and measurements of the first 340 women enrolled in the study. Women were enrolled 5-28 months after their initial breast cancer diagnosis (median, 10 months), and 4-28 months after their axillary lymph node surgery (median, 9 months). Seven women who had had bilateral breast cancer and axillary dissection and 1 woman who declined measurement were excluded from subsequent analyses. At interview, 121 women (36.5%) reported that they had experienced swelling of the surgery-side arm for two weeks or longer, and 108 reported current swelling. For 48 women (14.5%), the calculated volume of the surgery-side arm was > 200 ml larger than the contralateral arm. This included 21 (9.5%) of the women who reported no current swelling and 27 (25.0%) of the women who reported current swelling. Increasing body mass was associated with lymphedema identified either by self-report or by calculated arm volume. Relative to women with a body mass index (BMI) < 25, the odds ratios and 95% confidence intervals for lymphedema based upon self-report and arm measurement, respectively, among women with a BMI > 30 were 1.6 (0.9-2.9) and 4.5 (2.0-10.4).

Future analyses in this study cohort will assess changes in arm volume over time and relationships with treatment and lifestyle factors. As increasing numbers of women with breast cancer survive their illness, identifying evidence-based strategies to minimize the long-term consequences of treatment, such as lymphedema, is increasingly important.

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