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Introduction

There is a growing body of epidemiological literature supporting the positive relationship between a woman's endogenous lifetime hormone exposure and the risk of breast cancer. Specifically, early menarche and late menopause are associated with increased risk of breast cancer, and this risk is reduced by surgical oophorectomy in the premenopause. Breast cancer adjuvant treatments often lead to premature menopause, and this may be an important factor in the efficacy of these treatments in younger women. However, women who experience premature menopause are at increased risk of earlier cardiovascular disease, as well as premature osteoporosis. Further, numerous epidemiological studies support the benefits of supplemental estrogen therapy in the postmenopause as an effective means of reducing mortality from both cardiovascular disease and osteoporotic fractures. There is uncertainty about how all of these factors play out in breast cancer survivors who have experienced premenopausal disease. Therefore, the primary focus of this cross-sectional study is to examine gonadal function and reproductive health comprehensively in long-term survivors of breast cancer.

Specific Aims

1. To recruit a sample of breast cancer survivors (BCS) who were 50 years or younger at diagnosis, and were treated initially at the Jonsson Comprehensive Cancer Center at UCLA between 1994 and 1997.

2. To recruit additional subjects with identical characteristics treated at Kaiser Permanente West Los Angeles or Kaiser Permanente Sunset between 1989 and 1997.

3. To survey these BCS to determine the effects of past treatment on menstrual history patterns and fertility, as well as past and current menopausal symptoms, and current health-related quality of life.

4. To measure current reproductive hormone status, cardiovascular lipid profiles, body composition and bone mineral density in these BCS to assess the late effects of breast cancer treatment on risk factors for coronary artery disease and osteoporotic fractures.

Description of Phases 1 and 2

The study is being conducted in two phases. In phase one, the UCLA Medical Center Tumor Registry and the Kaiser Permanente Tumor Registry are being used to identify a group of breast cancer survivors who were 50 years or younger at the time of diagnosis and who are currently disease free. Eligible breast cancer survivors are then invited to participate in study that will ask them to complete a survey questionnaire that reviews their menstrual and reproductive history, medication history (including past and current use of contraceptive and non-contraceptive hormones), pregnancy/fertility history, past and current symptoms that may be menopause related, use of alternative therapies, diet and physical activity levels, as well as standardized measures of health-related
quality of life. The survey also asks detailed information about each subject's cancer treatment, including type and duration of chemotherapy and hormone therapy received. In addition to analyzing the results from the survey, we will examine the medical and demographic characteristics of breast cancer survivors who participate in comparison with those who refuse.

In phase two of the research, all breast cancer survivors who completed the phase one survey questionnaire are invited to come to UCLA for an in-person visit to complete physical and laboratory studies. These include blood work for evaluation of cardiovascular lipids and gonadal hormones; measurement of blood pressure, height, weight and waist/hip girth; and performance of a bone mineral density test. The results of the questionnaire data and medical treatment details from phase one, as well as current gonadal hormone levels, will be used to explore the predictors of current health status/health-related quality of life, cardiovascular lipids, and bone mineral density. The analyses planned will examine whether a relationship exists between menstrual patterns after breast cancer and current health-related quality of life, lipid profiles, bone mineral density or body composition. These data will be useful in the management of women who are currently long-term survivors of breast cancer, and can be used to provide supporting pilot data for the design of a prospective longitudinal study examining the impact of breast cancer treatment on the long-term reproductive health of premenopausal women with breast cancer.

This study will add to prior data from an NIH-funded study, in which women 5-10 years after diagnosis (as identified by the UCLA Tumor Registry) completed phases 1 and 2 as described above. This current study will enlarge the sample size substantially by adding additional long-term survivors (5-10 years post diagnosis) identified by the Kaiser Tumor Registry, as well as short-term survivors (2-5 years post diagnosis), identified by both the UCLA and Kaiser Tumor Registries. We are currently in the process of inviting long-term Kaiser survivors and short-term UCLA survivors, as we have only recently received contact information for the short-term Kaiser survivors.

Progress report on first year of funding

Recruitment and Subject Characteristics

During the past year, we have obtained from the UCLA and Kaiser Tumor Registries contact information for 1,093 women (522 short-term survivors from UCLA, 192 short-term survivors from Kaiser, and 379 long-term survivors from Kaiser) who were diagnosed with breast cancer before the age of 50.

Between March 18, 1999 and September 30, 1999, we sent invitation letters to 339 breast cancer survivors (236 short-term survivors identified by UCLA and 103 long-term survivors identified by Kaiser) for phase 1 of the study. Of these, 78 letters were returned to sender (23%). From the remaining 261 potentially contactable women, we received 200 responses (77%), and of those women, 158 were interested in receiving a
screening call (79%). Caucasian women expressed the most interest in hearing more about the study (83%), followed by African American women (77%), Asian women (65%) and Hispanic women (62%).

As of October 1, 1999, 155 women have been screened for this phase of the study. Of those, 8 women were found to be not eligible, 2 refused during the screening call, 113 women successfully completed the questionnaire, and the remaining questionnaires are pending.

For phase 2, we are approaching women who completed a questionnaire and who live in California to come in for an in-person visit, which includes a blood draw to measure cholesterol and hormone levels, and a BMD to measure bone mineral density. As of October 1, 1999, we mailed out 33 invitation letters for this second phase of the study. We have thus far telephoned 23 of these women to ascertain interest in the study, and 19 women have agreed to participate.

Currently, 7 women have completed the appointment; 6 were post-menopausal and 1 was pre-menopausal. The pre-menopausal woman agreed to complete the menstrual diary calendars, in which a woman checks off her daily symptoms (bleeding, bloating, hot flashes, irritability, and joint aches) every day for a year.

Summary and Plans For the Next Year

As of October 1, 1999, we have sent out invitation letters to 103 long-term survivors and 236 short-term survivors. We have contact information for an additional 276 long-term survivors, and an additional 478 short-term survivors. We plan to continue inviting women steadily throughout the next year.

With completion of data collection on the long-term survivors, we plan to begin analysis of data on reproductive health, quality of life, gonadal hormone status, lipids and bone density.