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INTRODUCTION

Risk reducing surgery remains an important option for women at risk for ovarian cancer, yet the quality of life implications of such surgery are vastly understudied. Our effort to prospectively study women who choose prophylactic surgery is providing much-needed feedback for other women who seek counseling regarding cancer risk reduction strategies. Further, comparing women undergoing surgery with a control group of those who opt not to pursue it provides a more rigorous scientific perspective to support clinical management.

With the approval of an additional one-year no-cost extension we will be able to fully monitor new participants in the control group, providing matched groups for final analysis. Future analysis will support the development of an educational booklet, funded by the Sandy Rollman Ovarian Cancer Foundation, Inc., to provide to women considering prophylactic surgery the information they need to make an informed decision.

BODY

The following describes the progress during the past year associated with each task in the Statement of Work.

Task 1: Creation of Participant Advisory Board

We continue with an informal advisory approach, holding consultations by telephone or on a person-to-person basis. A Gynecologic Oncology Clinical Trials Working Group continues to meet monthly under the direction of Dr. Mitchell Edelson and our staff participates regularly. This forum allows networking and discussion of recruitment strategies. We continue our networking relationship to several local advocacy groups, including the Philadelphia chapter of the National Ovarian Cancer Coalition and The Sandy Rollman Ovarian Cancer Foundation, Inc.

Task 2: Selection of Survey Instruments

There have been no changes in the survey instruments previously approved by the IRB. Outcome variables include physical functioning, menopausal symptoms, body image, sexual functioning, anxiety, depression, and use of pharmaceutical, dietary and alternative therapies. The instruments being used are as follows:

1. The NSABP BCPT Quality of Life Questionnaire. This instrument was used by over 13,000 women in the Tamoxifen prevention trial. It includes the Medical Outcomes Study (MOS) 36-item short form, a generic measure of health-related QOL, the Center for Epidemiologic Studies-Depression Scale, used widely in community epidemiologic studies, the MOS sexual problems scale, and a 43-item symptom checklist of commonly reported physical and psychologic symptoms, as well as symptoms associated with the menopause, including the domains of vasomotor symptoms, vaginal dryness, sexual functioning, sleep disturbance and cognitive

functioning. Sleep patterns and sleep quality may be disrupted by surgical menopause. This questionnaire is collected at all time points.

2. Post-Surgical Expectations Questionnaire. The NSABP BCPT Quality of Life Questionnaire has been modified to assess women's expectations of menopausal symptoms they anticipate experiencing following oophorectomy. It includes an open-ended response format as well as a Likert-type summary scale of symptoms. This questionnaire is only assessed at baseline, prior to surgery.
3. Fallowfield Sexual Activity Questionnaire (SAQ). This tool is a validated measure for describing the sexual functioning of women in terms of activity, pleasure and discomfort. It was developed to investigate the impact of long-term Tamoxifen usage on the sexual functioning of women at high risk of developing breast cancer. This measure is collected at all time points.
4. Self Concept Scale. This 10-item scale assesses the participants' satisfaction with different areas of their body and their overall weight. Persons undergoing oophorectomy may experience an alteration in their perception of their body image, which may affect their psychosocial status and intimate relationships. This scale was developed by Dr. David Cella, (Director, Center on Outcomes Research and Education, Evanston Hospital) through his work with breast cancer patients. It is collected at all time points.
5. Medical/Dietary Supplement Survey. This survey elicits use of hormone replacement therapy, dietary supplements, micronutrients, as well as exercise, yoga, meditation, and other forms of coping strategies. The survey has been piloted among 48 women in the FRAP program for feasibility and ease of administration. Overall, we found that 89% of the women surveyed took some form of dietary supplement. It is collected at all time points.
6. Post-Surgery Satisfaction Questionnaire. Patients' levels of satisfaction with oophorectomy will be assessed using three items rated on a 5-point Likert-type scale. Scores from the three items will be combined to form a composite index of satisfaction. It is collected at all post-surgery time points.
7. Medical Outcomes Survey. This survey will capture information on new medical diagnoses, procedures, and screening exams at the 12-month follow-up time point. It is adapted from our current FRAP annual follow-up questionnaire.

Task 3: Development of a Recruitment Strategy

A new recruitment strategy was employed to boost control group enrollment. We approached participants in our Ovarian Cancer Consortium for Research and Surveillance from collaborative institutions, such as Wake Forest University Baptist Medical Center and Cooper Medical Center, such that now the two study groups are matched in size. The surgery arm now includes 38 women and the control group 34. Additionally a recruitment summary was posted on www.facingourrisk.org, website for FORCE (Facing Our Risk of Cancer Empowered), a nonprofit organization for women whose family history or genetic status puts them at high risk of getting ovarian cancer. Compliance with all study time point surveys is relatively consistent. Enrollment will end 9/30/04.

Task 4: Creation of Data Entry Screens, Data Editing Program

This task is completed and data entry is a smoothly flowing process. Data is entered promptly and close consultation between the project manager and data entry clerk has served to oversee data editing review. A series of edit checks and quality assurance measures take place on a routine basis whenever data is entered into our bioinformatics system.

Task 5 & 6: Conduct Baseline & Follow-up Surveys

Surveys are sent in packets with an instruction cover letter and postage paid return envelope. The project manager receives an email notice to trigger the sending of packets. Reminder postcards and personal phone calls are made when warranted to alert participants of overdue surveys.

Task 7: Data entry, data analysis

Data entry is up to date. The project manager tracks study accrual and questionnaire completion on a biweekly basis. Interim analysis has yielded the outcomes reported below.

Task 8: Report, manuscript preparation

The required application for ongoing review by the Research Review and IRB committees at Fox Chase Cancer Center was prepared and approved on 3/29/04. The principal investigator, Dr. Mary Daly, presented interim analysis to the Population Science Meeting at Fox Chase Cancer Center on 3/23/04. Insufficient data exists at this time for manuscript preparation.

KEY RESEARCH ACCOMPLISHMENTS

- No significant differences in selected sample characteristics regarding median age, race, or education level. The surgery had more married women and women who had had *BRCA* gene testing (**See Table 1**).
- Relative to the Quality of Life measures (NSABP BCPT Quality of Life questionnaire) there were significant differences at one month between the surgery and control groups in the following measures: the surgery group had a higher percentage of sample experiencing hot flashes ($p=0.0002$), constipation ($p=0.02$), decrease in appetite ($p=0.02$), and night sweats ($p=0.004$). Likewise the surgery group had more limitation of daily activities (physical functioning, $p=0.03$), more alteration in work or daily activities (role functioning, physical $p<0.0001$), and more interference in social functioning ($p=0.001$). The surgery group also had more bodily pain ($p=0.01$), and less vitality ($p=0.05$) when compared with the control group. The statistically significant difference between the two groups reporting hot flashes persisted at six months ($p=0.05$) and in reporting vaginal dryness which persisted at six and twelve months ($p=0.004$, $p=0.003$) (**See Table 2**).
- Regarding sexual activity, there was no difference in percentage of women engaging in sexual activity but at one month there was a significant decrease in pleasure in the surgery group ($p=0.04$). The surgery group's increased pain during sexual activity reached statistical significance at all time points ($p=0.001$, $p=0.04$, $p=0.001$, $p=0.05$). Further the frequency of

sexual activity was less than usual at one month in the surgery group ($p < 0.0001$) (See Table 3).

- There was no significant difference in self-concept at either baseline or one month between the surgery and control groups (See Table 4).

REPORTABLE OUTCOMES

Table 1 Sample Characteristics		
	Surgery n (%)	Control n (%)
<u>Age (median)</u>	45.5 yrs	43 yrs
<u>Race</u>		
Caucasian	36 (94%)	32 (94%)
<u>Education</u>		
Some College	30 (81%)	26 (81%)
<u>Marital Status</u>		
Married	30 (81%)	21 (66%)
Never Married	4 (11%)	5 (16%)
Divorced	3 (8%)	6 (18%)
		p=0.03
<u>BRCA Gene mutation status</u>		
Positive	14 (37%)	10 (30%)
Indeterminate	19 (50%)	14 (40%)
Not tested	5 (13%)	10 (30%)
		p=0.01

Table 2 Quality of Life Measures

	Baseline		1 month		6 month		12 month	
	Surgery	Control	Surgery	Control	Surgery	Control	Surg	Cont
Everyday problems during the past 4 weeks	50%	29%	70%	21%	62%	31%	67%	47%
% reporting hot flashes				p=0.0002		p=0.05		
% reporting headaches	62%	48%	45%	71%	52%	69%	63%	67%
				p=0.04				
% reporting constipation	21%	26%	45%	18%	35%	25%	22%	47%
				p=0.02				
% reporting vaginal discharge	29%	29%	24%	18%	10%	18%	7%	40%
								p=0.02
% reporting vaginal dryness	44%	10%	24%	11%	48%	6%	52%	7%
		p=0.002				p=0.004		p=0.003
% reporting cramps	21%	32%	12%	25%	10%	38%	0%	60%
								p=0.00001
% reporting breast sensitivity	24%	45%	9%	29%	14%	44%	19%	40%
				p=0.05		p=0.03		
% reporting decrease in appetite	12%	6%	36%	11%	14%	6%	11%	0%
				p=0.02				
% reporting night sweats	38%	23%	58%	21%	41%	25%	48%	27%
				p=0.004				
Physical Functioning	91.5	81.3	72.2	81.3	81.5	92.2	83.3	91.3
				p=0.03				
Role Functioning (physical)	81.7	83.1	32.5	77.8	80.4	92.2	81.5	80
				p<0.0001				
Social Functioning	89.3	84.7	59.5	77.2	91.5	86.7	81.9	82.5
				p=0.001				
Bodily Pain	71	64.2	49.3	63.6	67.9	76.3	61.1	70.7
				p=0.01		p=0.03		
Vitality	56.1	52.4	46.4	55	58.8	53.8	58.7	58
				p=0.05				

	Baseline		One month		6 month		12 month	
	Surgery	Control	Surgery	Control	Surg	Cont	Surg	Cont
% engaging in sexual activity	79%	73%	53%	57%	79%	75%	73%	73%
Pleasure score	13.5	14	11.9	14.7 p=0.04	12.8	13.7	12.9	13.9
Pain score	4.7	3.1 p=0.001	4.6	3.2 p=0.04	5.2	2.8 p=0.001	4.6	3.5 p=0.05
Comparison of sexual frequency with what is normal for participant	2.1	2.2	2.7	2 p<0.0001	2.4	2.2	2.3	2.1

	Baseline		One month		6 month		12 month	
	Surgery	Control	Surgery	Control	Surg	Cont	Surg	Cont
Satisfaction with body score	24.9	25	26.7	25.9	26.4	25.4	26.3	25.8
Importance of breast appearance	2.6	2.7	2.5	2.6	2.3	2.7	2.4	2.5
Self concept of weight	1.4	1.5	1.4	1.5	1.3	1.4	1.4	1.4

CONCLUSIONS

Pertinent findings from interim analysis of selected measures are reported here comparing surgery and control groups at all time points. An effective recruitment strategy in the past year has boosted control group enrollment to afford matched groups. The coming year will allow for completion of data collection and final comprehensive analysis to determine changes in quality of life over time and between the two groups. Important findings from interim analysis presented here show statistically significant short term differences between groups with the surgery group experiencing more hot flashes, night sweats, decrease in physical and social functioning and decrease in sexual activity frequency and pleasure. There is no difference in self-concept between groups.

The differences in key areas of quality of life and sexual activity after surgery are already being incorporated into our counseling of women considering risk-reducing surgery. Our current project to develop a decision-making booklet for women considering prophylactic surgery is underway with a professional writer on board. This study's outcomes will be directly translatable to the women who need this important information to develop coping strategies for increased risk of ovarian cancer.

REFERENCES

None

APPENDICES

None