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Acceptability of prophylactic salpingectomy with delayed oophorectomy as risk-reducing surgery among BRCA mutation carriers

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HIGHLIGHTS

- BRCA mutation carriers are willing to participate in a PSDO trial.
- The majority of participants found potential PSDO study risks to be acceptable.
- These results suggest that adequate accrual for a clinical trial of PSDO is possible.

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ABSTRACT

Objective. Given the emerging evidence for the fimbria as the site of origin for many serous carcinomas in BRCA mutation carriers, consideration is being given in studying prophylactic salpingectomy with delayed oophorectomy (PSDO) as a risk-reducing surgery. We aimed to determine the interest in a study of PSDO among these women.

Methods. We evaluated the results of an online survey conducted by Facing Our Risk of Cancer Empowered (FORCE), a patient advocacy group, from October 2010 to August 2012. Premenopausal BRCA mutation carriers with no history of ovarian cancer or prior bilateral salpingo-oophorectomy (BSO) were included.

Results. Of the 204 women meeting inclusion criteria, median age was 35 years, 92.5% were white, 25.7% were Jewish, and 16.7% had a history of breast cancer. Overall, 34.3% reported interest in a study of salpingectomy, 35.3% were unsure, and 30.4% were not interested in the study. Women noted the possibility of lowering ovarian cancer risk without menopause as a compelling reason to participate (83.8%). Reasons for not participating in a salpingectomy study included surgical complications (46.6%), potential ovarian damage (42.2%), planning BSO soon (32.4%), and surgical costs (32.8%). Acceptable study risks included the need for two surgeries (77.2%), possibility of not lowering ovarian cancer risk (68%), and disruption of ovarian blood supply (66.5%).

Conclusions. One-third of BRCA mutation carriers indicated definite interest in a PSDO study. Potential study risks were acceptable to most women. These findings suggest that patient accrual for a clinical trial of prophylactic salpingectomy with delayed oophorectomy is possible.

Introduction

Of the 22,000 ovarian cancer cases diagnosed in 2013, approximately 10% can be attributed to an inherited predisposition [1,2]. The most common hereditary cause of ovarian cancer is a mutation in the *BRCA1* or *BRCA2* genes. Women who have a *BRCA1* mutation have a 39% to 46% risk of developing ovarian cancer by age 70, while women with a *BRCA2* mutation carry a 10% to 27% risk by age 70 [3]. In contrast, women in the general population have a 1.4% lifetime risk of developing ovarian cancer [4].

The National Comprehensive Cancer Network (NCCN) has developed guidelines to aid with the management of these high-risk women. These guidelines state that risk-reducing salpingo-oophorectomy (RRSO) should be recommended to BRCA mutation carriers between the ages of 35 to 40, or when childbearing is complete [5]. RRSO provides a 75% to 96% reduction in ovarian cancer risk and is the most efficacious method of ovarian cancer prevention for these women [6–9]. RRSO also appears to provide a survival advantage as studies have demonstrated a 60% to 70% decrease in overall mortality among BRCA mutation carriers who have undergone the procedure compared with those who have not [10,11].

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Though RRSO has profound benefits, there are significant concerns regarding the adverse effects of surgical menopause on these young women. Oophorectomy prior to natural menopause is associated with an increased risk for osteoporosis, cardiovascular disease, cognitive impairment, and overall mortality [12–14]. Furthermore, women who undergo RRSO before menopause experience significant changes in sexual functioning as well as vasomotor symptoms [15]. These side effects can lead BRCA mutation carriers to avoid RRSO.

Since the adoption of RRSO for BRCA mutation carriers in the 1990s, thousands of women have undergone the procedure. The study of their pathology specimens has resulted in the discovery of a small number of occult malignancies. The majority of these tumors have been located in the fallopian tube [16–23]. These findings have led to the hypothesis that the fallopian tube is the true site of origin of many BRCA-associated high-grade serous pelvic malignancies. This theory, along with the risks associated with early menopause, has brought increasing interest to the role of salpingectomy with delayed oophorectomy (PSDO) as a potential alternative to RRSO for BRCA mutation carriers [24,25].

PSDO is an investigational surgical strategy where women decrease their risk of ovarian cancer, but delay the side effects associated with menopause. Women who undergo PSDO would have both of their fallopian tubes removed upon completion of childbearing, but oophorectomy would be performed as a separate surgical procedure at a later date. Though some researchers have expressed enthusiasm for PSDO, it is unknown how BRCA mutation carriers perceive the procedure. The objective of this study was to determine the acceptability of and interest in a clinical trial of PSDO among BRCA mutation carriers.

Materials and methods

Between October 2010 and August 2012 an online survey was conducted by Facing Our Risk of Cancer Empowered (FORCE). FORCE is a patient advocacy group for women with hereditary breast and ovarian cancer. The survey was developed by FORCE and administered on their website. The survey assessed participants' beliefs about PSDO as a form of ovarian cancer prevention (Supplementary material). Demographic information and medical history were also collected, but participants were not asked to provide personal identifiers. This study was approved by the Institutional Review Board (IRB) of The University of Texas MD Anderson Cancer Center. As no protected health information was collected, a waiver of informed consent was granted by the IRB.

The online survey was available to all visitors to the FORCE website during the study period and was promoted through FORCE's social media pages, website, and electronic newsletter. However, to limit this study to women who would be eligible for a PSDO trial, only premenopausal BRCA mutation carriers were included in the analysis. Women who reported prior bilateral salpingo-oophorectomy or a history of ovarian, fallopian tube, or primary peritoneal carcinoma were also excluded.

Demographics and medical history of participants were summarized using descriptive statistics, including medians, means, standard deviations, ranges, and frequencies. Chi-square tests were used to compare differences between groups. IBM SPSS Statistics for Windows, Version 19.0, was used for statistical analysis (IBM Corp., Armonk, NY). A two-sided p value of less than 0.05 was considered statistically significant.

Results

Of the 488 women who completed surveys, 204 met inclusion criteria and were included in a further analysis. Table 1 details the characteristics of these women. When queried about their desire to participate in a study of PSDO, approximately one-third of the respondents (34.3%) reported definite interest. An additional 35.3% of women were unsure if they would participate in this type of study, although many requested more information about PSDO in their survey comments. When asked about reasons to participate in a PSDO study, 83.8% of women agreed that it was the possibility of lowering ovarian cancer risk without menopause. The majority of participants (84.2%) also agreed that helping to further ovarian cancer research for high-risk women was an important reason to participate. Overall, potential PSDO study risks were acceptable to the majority of survey participants (Table 2).

Table 1
Demographic characteristics of participants (N = 204).

Age	Years
Median (range)	35 (21–53)
Mean	35.4
Race	% (n)
White	90.7 (185)
Hispanic	3.4 (7)
Other	3.9 (8)
Unknown	2 (4)
Ashkenazi Jewish	% (n)
	25.7 (52)
Education	% (n)
Some high school	0.5 (1)
High school graduate	2.5 (5)
Some college	13.7 (28)
Bachelor's or advanced degree	82.4 (168)
Unknown	1 (2)
BRCA status	% (n)
BRCA 1 mutation	62.3 (127)
BRCA 2 mutation	37.7 (77)
Parity	% (n)
Parous	57.4 (117)
Nulliparous	41.2 (84)
Unknown	1.5 (3)
Cancer history	% (n)
No History	83.3 (170)
Breast cancer history	16.7 (34)

Sixty-one women (30.3%) stated that they were not interested in participating in a PSDO study. When all respondents were queried regarding reasons to not participate in a PSDO study, 46.6% cited surgical complications, 32.8% reported surgical costs, and 14.7% noted anesthesia concerns. Additionally, 32.4% of women did not want to participate because they already planned to undergo RRSO.

Comparisons of risk acceptability were made between women who were interested in a PSDO study and those who were not interested (Table 3). As expected, women who were interested in a PSDO trial were more likely to find the study risks to be acceptable as compared with women who were not interested in a PSDO study.

Post-hoc subgroup analyses were performed on the surveys of nulliparous and parous women. There was no difference between the groups in the number of women interested in participating in a PSDO study (parous 37.9% vs nulliparous 29.8%, $p = 0.42$). Parous women were more likely than nulliparous women to find the possibility of undergoing two surgical procedures (28.9% vs 15.1%, $p = 0.04$) and the potential to not lower their ovarian cancer risk (39.2% vs 22.1%, $p = 0.02$) unacceptable. However, nulliparous women were more likely to report concerns about potential disruption of ovarian blood supply as a reason to not participate in a PSDO trial (52.9% vs 34.2%, $p = 0.01$).

As ovarian cancer risk differs among BRCA1 and BRCA2 mutation carriers, analysis was also performed on the survey responses of these two groups. There were no statistically significant differences between these groups in any of the survey responses, including the acceptability of disruption of ovarian blood supply (68.9% vs 62.5%, $p = 0.4$), acceptability of requiring two procedures (78% vs 74.2%, $p = 0.58$), and acceptability of the potential for surgery to not lower ovarian cancer risk (72.1% vs 60.9%, $p = 0.13$).