Randomized Controlled Trial of a Psychosocial Telephone Counseling Intervention in BRCA1 and BRCA2 Mutation Carriers

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Abstract

Background: Responses following BRCA1/2 genetic testing are relevant for the comprehension of risk status and may play a role in risk management decision making. The objective of this study was to evaluate a psychosocial telephone counseling (PTC) intervention delivered to BRCA1/2 mutation carriers following standard genetic counseling (SGC). We examined the effect of the intervention on distress and the concerns related to genetic testing.

Methods: This prospective randomized clinical trial included 90 BRCA1/2 mutation carriers. We measured anxiety, depression, and genetic testing distress outcomes at intervention baseline and 6 and 12 months following disclosure. We evaluated the effects of SGC versus SGC plus PTC on psychological outcomes using intention-to-treat analyses through generalized estimating equations.

Results: At 6 months, PTC reduced depressive symptoms ($Z = -2.25, P = 0.02$) and genetic testing distress ($Z = 2.18, P = 0.02$) compared with SGC. Furthermore, women in the intervention condition reported less clinically significant anxiety at 6 months ($\chi^2 = 4.11, P = 0.04$) than women who received SGC. We found no differences in outcomes between the intervention groups at the 12-month follow-up.

Conclusions: As an adjunct to SGC, PTC delivered following disclosure of positive BRCA1/2 test results seems to offer modest short-term benefits for distress and anxiety. These results build upon a growing literature of psychosocial interventions for BRCA1/2 carriers and, given the potential impact of affect on risk management decision making, suggest that some carriers may derive benefits from adjuncts to traditional genetic counseling.

Introduction

Genetic counseling and testing for BRCA1 and BRCA2 (BRCA1/2) mutations have become standard care in the clinical management of women with a family history suggestive of hereditary breast or ovarian cancer (1). Although receipt of positive BRCA1/2 genetic test results does not lead to long-term clinically relevant distress (2–5), numerous studies document both short-term and ongoing distress in some mutation carriers (e.g., younger women and those with high pretest anxiety; refs. 6–9).

Emerging evidence shows that an individual’s emotional state can affect decision making around risk information (10). Thus, even subclinical or transient increases in distress following BRCA1/2 testing could potentially influence decisions about management of breast and ovarian cancer risks (11). For example, distress has been identified as a predictor of prophylactic surgery decisions among mutation carriers (12). Moreover, women who have undergone BRCA1/2 testing rate management decision making as highly stressful (11, 13, 14). Interventions are now being developed to address psychosocial concerns and provide risk management decision support during and after receipt of BRCA1/2 test results (15–18). These interventions have led to decreases in depressive symptoms (16), reduced cancer worries (15), and greater information seeking and uptake of prophylactic oophorectomy (17). Moreover, BRCA1/2 mutation carriers
who were undecided about risk management reported improved psychosocial outcomes following use of a decision aid (18). These prior interventions have included individuals regardless of BRCA1/2 test result or focused exclusively on decision support.

To date, no research has evaluated an adjunct intervention designed exclusively for BRCA1/2 carriers to address psychosocial concerns. In the present study, we developed a postdisclosure psychosocial telephone counseling (PTC) intervention to address psychological reactions to receiving positive BRCA1/2 test results. The intervention was based on the Transactional Model of Stress and Coping (19), which posits that an individual’s adjustment to a stressor is driven, in part, by their appraisal of the stressor as threatening and their ability to manage the stressor. We hypothesized that the PTC intervention would lead to improved psychological functioning compared with standard genetic counseling (SGC), with improved functioning moderated by perceptions of stress and confidence related to managing genetic testing stressors. Evaluating the effect of disseminable interventions for BRCA1/2 carriers will provide additional information on the value of these programs for psychosocial outcomes and risk management decisions in this population.

Patients and Methods

Study Population

Participants were female BRCA1/2 mutation carriers ages 18 y and older identified through genetic counseling and testing programs in Washington, DC and Toronto, Canada. Women with metastatic disease or recurrent ovarian cancer and those who did not read and speak English were ineligible for this study. Genetic counseling and testing and PTC were provided free of charge. The institutional review boards at both centers approved the research protocol. All women provided written informed consent for study participation at the pretest genetic counseling session.

Design and Procedures

The procedures for this study have been described in detail in previous reports (20, 21) and are summarized here. We contacted potential participants by telephone to determine eligibility and complete a pretest questionnaire assessing sociodemographics, personal and family history of cancer, and psychological functioning. Participants attended standardized pretest education and posttest results disclosure sessions conducted by a genetic counselor.

One month after the disclosure of BRCA1/2 test results, but before notification of intervention group assignment, we contacted participants for a follow-up telephone interview to assess psychological functioning. This interview served as the baseline (preintervention) assessment. Interviewers informed participants of their study assignment at the end of this assessment. BRCA1/2 mutation carriers were randomized to receive SGC only or SGC plus PTC (see Fig. 1). A computer-generated randomization program stratified intervention assignments by study site. We assigned mutation carriers from the same family to the same intervention group and PTC counselor. Participants completed follow-up interviews 6 and 12 mo after receipt of their test results.

Counseling Protocols

Standard Genetic Counseling (SGC). The pretest education session included a discussion about hereditary breast and ovarian cancer, mutation testing, and the potential benefits, limitations, and risks of genetic testing. The disclosure session included disclosure of test results, information about the risks of developing cancer, and individualized management strategies. Participants received a written summary letter and a standard follow-up call from their genetic counselor 2 wk after disclosure.

Standard Genetic Counseling plus Psychosocial Telephone Counseling (SGC plus PTC). The PTC protocol included all aspects of SGC. Following the completion of SGC, individuals randomized to PTC also received a PTC intervention. The PTC intervention consisted of five weekly telephone counseling sessions delivered by trained and supervised Master’s level mental health counselors (22). Intervention materials were mailed to PTC participants before the first session and included four booklets: “Emotional Responses to Genetic Testing,” “Making Medical Decisions,” “Managing Family Concerns,” and “The CARE Workbook: Strategies to Help Cope with Stressors Related to Your Genetic Test Result.”

To facilitate the transfer from SGC to the PTC intervention, genetic counselors provided PTC counselors with case notes and reports, and spoke with the PTC counselor about the participant’s primary concerns about medical decision making, family issues, and emotional reactions. PTC counselors then contacted participants to orient them to the intervention and schedule the five sessions.

The first session of PTC consisted of a semistructured clinical interview to elicit the participants’ reactions to their test results. Sessions 2 to 4 were individualized to the specific concerns raised by each participant during their disclosure session and PTC session 1. Although participants from the same family were assigned to the same PTC counselor, counselors did not share information that had been provided by other relatives. Specific coping strategies (e.g., problem solving, role playing) tailored to each participant’s needs were developed and applied during sessions 2 to 4. The final session focused on integration/closure and development of a plan to execute goals.

Measures

Covariates. We obtained demographic and clinical information during the pretest telephone interview. We assessed age, marital status, income, education, employment, and personal/family history of cancer.

Moderators

Appraisals: Perceptions of Stress and Confidence. We used the perceived stress and confidence scales (23) to evaluate
whether primary (stress) and secondary (confidence) appraisals moderate the effect of the PTC intervention on distress. Both scales consisted of 5 items, with responses made on a four-point Likert-style scale. Both scales also had adequate internal consistency in the present study (perceived stress $\alpha = 0.73$; perceived confidence $\alpha = 0.79$).

**Outcome Variables**

**Primary Distress Outcomes: Anxiety and Depression.** We measured anxiety and depression using the Hopkins Symptom Checklist (HSCL-25; ref. 24). The HSCL-25 is a 25-item Likert-style instrument that evaluates the presence and severity of anxiety and depressive symptoms during the past month. The anxiety (10 items) and depression (13 items) subscales are each answered on four-point scales (1, “Not at All” to 4, “Extremely”). We did not use the two somatic items from the scale. Internal consistency in the present study was $\alpha = 0.82$ and $\alpha = 0.87$ for the anxiety and depression subscales, respectively. We calculated an overall distress score by combining the subscale scores. Clinically significant levels of anxiety, depression, and overall distress were calculated by dividing the sum of each subscale by the number of items, with scores above 1.75 defined as clinically significant (25).

**Secondary Distress Outcomes: Genetic Testing Concerns.** We used the Multi-Dimensional Assessment of Cancer Risk Assessment (MICRA) scale to evaluate emotional responses to BRCA1/2 test results (6). The MICRA is a 21-item Likert-style scale that assesses affective...
responses to receiving BRCA1/2 test results. The MICRA has shown solid validity and reliability in prior research (6), and had good internal consistency in the present study ($\alpha = 0.84$).

**Data Analysis**

We compared the two study arms on sociodemographics and baseline distress using $\chi^2$ tests for categorical variables and Wilcoxon tests for continuous measures because of non-normal distribution of the appraisal and distress variables at baseline. Log and square root transformations were not successful in creating normal distributions for these variables. We also used Wilcoxon tests to identify demographic factors associated with baseline levels of outcome measures and $\chi^2$ and t tests to identify demographic factors associated with study retention and completion of the PTC intervention. We used t tests to evaluate differences in outcomes between study arms at each time point, as t tests seem to be robust against most violations of normality (26). To identify the effect of the intervention on clinically significant anxiety, depression, and overall distress, we used a $\chi^2$ test comparing “cases” to “noncases” across study arms. Finally, to evaluate the independent effect of study arm on distress at 6 and 12 mo, we conducted multiple linear regression analyses using generalized estimating equations to control for intraclass correlations. As appropriate, we included baseline levels of each outcome and control variables in the regression models. We evaluated whether the stress or confidence appraisal variables moderated the effect of the intervention on psychosocial outcomes by entering an interaction term into the regression models. We adjusted for multiple comparisons (27) and used an intention-to-treat approach in which we included all participants regardless of whether they completed the intervention. To help inform the design of future cluster randomized trials, we estimated the intraclass correlation coefficient (ICC) for the 6-mo psychological outcomes (28).

**Results**

A total of 575 eligible women were identified, and of these, 435 (76%) participated in genetic counseling and received BRCA1/2 test results (Fig. 1). Of the 435 women who received BRCA1/2 test results, 128 were identified as mutation carriers eligible for study participation. Eligible women were randomized to PTC ($n = 68$ women, 46 families) or SGC ($n = 60$ women, 46 families; see Fig. 1). The two arms did not differ on sociodemographic characteristics or baseline psychological functioning.

Fifty (76%) PTC participants completed all five telephone sessions, 3 (4%) completed one to four sessions, and 13 (22%) declined to participate in the intervention. On average, participants initiated the first counseling session 37.9 days (SD, 23.4 days) after the intervention baseline assessment and completed all five telephone sessions within 35 days (SD, 21 days). Prior work has described differences between intervention completers and non-completers (20). Seventy-two percent ($n = 43$) and 65% ($n = 39$) of SGC participants completed the 6- and 12-month follow-up assessments, respectively, compared with 69% ($n = 47$) and 65% ($n = 44$) of PTC participants. Women lost to follow-up had more years of education than women who remained in the study ($\chi^2 = 3.97, P = 0.046$). There were no other differences between these groups. We controlled for education in all outcome analyses. Final analyses included data from 90 participants for the 6- and 12-month follow-ups. As shown in Table 1, there were no differences in sociodemographic or clinical characteristics between study groups.

**Table 1. Characteristics of sample by intervention condition**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PTC ($n = 47$)</th>
<th>SGC ($n = 43$)</th>
<th>All ($n = 90$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\leq$50 y</td>
<td>36 (76.6)</td>
<td>32 (74.4)</td>
<td>68 (75.6)</td>
</tr>
<tr>
<td>&gt;50 y</td>
<td>11 (23.4)</td>
<td>11 (25.6)</td>
<td>22 (24.4)</td>
</tr>
<tr>
<td>Breast/ovarian cancer affected status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected</td>
<td>23 (48.9)</td>
<td>25 (58.1)</td>
<td>48 (53.3)</td>
</tr>
<tr>
<td>Unaffected</td>
<td>24 (51.1)</td>
<td>18 (41.9)</td>
<td>42 (46.7)</td>
</tr>
<tr>
<td>Proband status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proband</td>
<td>20 (42.6)</td>
<td>18 (41.9)</td>
<td>38 (42.2)</td>
</tr>
<tr>
<td>Relative</td>
<td>27 (57.4)</td>
<td>25 (58.1)</td>
<td>52 (57.8)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>36 (76.6)</td>
<td>35 (81.4)</td>
<td>71 (78.9)</td>
</tr>
<tr>
<td>Unmarried</td>
<td>11 (23.4)</td>
<td>8 (18.6)</td>
<td>19 (21.1)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some college/degree</td>
<td>35 (74.5)</td>
<td>30 (69.8)</td>
<td>65 (72.2)</td>
</tr>
<tr>
<td>No college</td>
<td>12 (25.5)</td>
<td>13 (30.2)</td>
<td>25 (27.8)</td>
</tr>
<tr>
<td>Employed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full time (%)</td>
<td>36 (76.6)</td>
<td>33 (76.7)</td>
<td>69 (76.7)</td>
</tr>
<tr>
<td>&lt;Full time (%)</td>
<td>11 (23.4)</td>
<td>10 (23.3)</td>
<td>21 (23.3)</td>
</tr>
<tr>
<td>Annual income*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;75,000 (%)</td>
<td>20 (45.5)</td>
<td>25 (59.5)</td>
<td>45 (52.3)</td>
</tr>
<tr>
<td>$\geq$75,000 (%)</td>
<td>24 (55.5)</td>
<td>17 (40.5)</td>
<td>41 (47.7)</td>
</tr>
</tbody>
</table>

NOTE: Affected, participants with a personal history of breast and/or ovarian cancer; unaffected, participants without a personal history of breast and/or ovarian cancer; proband, first person in the family to be tested for BRCA1/2; relative, a person who has BRCA1/2 testing who is a relative of someone positive for the BRCA1/2 mutation.

*Totals do not add to 90 in all cells due to a small amount of missing data on this variable.
Bivariate Comparison of Intervention Outcomes

Bivariate analyses revealed that PTC participants reported significantly lower depression scores at 6 months compared with SGC participants ($t(df=88) = 2.12, P = 0.02$). PTC participants were also less likely than SGC participants to report clinically significant levels of anxiety at 6 months (6.4% versus 20.9%, respectively; $\chi^2 = 4.11, P = 0.04$). Trends were evident for PTC participants to report lower levels of clinically significant depression ($\chi^2 = 3.43, P = 0.06$) and overall distress ($\chi^2 = 3.72, P = 0.05$) at 6 months. There were no differences between the SGC and PTC groups at 12 months on any study outcomes.

Multivariate Analysis of Psychological Outcomes

After adjusting for baseline psychological outcomes and other controlling variables (employment, education, income, and affected status), the intervention group had a significant independent effect on depressive symptoms ($Z = 2.25, P = 0.02$) and genetic testing distress ($Z = 2.18, P = 0.02$; see Table 2) at 6 months. Women randomized to the PTC group reported reduced depression and genetic testing distress at 6 months relative to the SGC group. We conducted identical general estimating equation multiple regression analyses for psychosocial outcomes at the 12-month follow-up and evaluated whether stress or confidence appraisals at 6 months moderated the effect of the PTC intervention on 12-month outcomes. Intervention group was not a significant predictor for any of the outcomes at 12 months, nor did the primary stress or secondary confidence appraisals moderate the effect of the intervention on study outcomes.

The cluster randomized trial included 90 women (observations) and 72 families (clusters), with an average of 1.25 observations per cluster. The estimated ICCs for the 6-months psychological outcomes were 0 for depressive symptoms, 0.07 for genetic testing concern, and 0.21 for anxiety symptoms. Following common practice, we set to 0 the estimated ICC for the 6-months depressive symptoms because we obtained a small negative estimate, and a negative ICC (that is, women from the same family are less similar to one another with respect to depressive symptoms than they are to women from another family) did not seem theoretically plausible.

Table 2. General estimating equation multiple regression analysis of 6-month psychological outcomes among BRCA1/2 mutation carriers ($n = 90$)

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Predictor variables</th>
<th>Parameter estimate</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline depression</td>
<td>0.66</td>
<td>4.58*</td>
</tr>
<tr>
<td>Deppressive symptoms</td>
<td>Employment status</td>
<td>−2.37</td>
<td>−1.30</td>
</tr>
<tr>
<td></td>
<td>Education level</td>
<td>2.00</td>
<td>1.52</td>
</tr>
<tr>
<td></td>
<td>Income level</td>
<td>0.16</td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td>Cancer history</td>
<td>0.80</td>
<td>0.77</td>
</tr>
<tr>
<td></td>
<td>Intervention group</td>
<td>−2.28</td>
<td>−2.25†</td>
</tr>
<tr>
<td>Anxiety symptoms</td>
<td>Baseline anxiety</td>
<td>0.57</td>
<td>5.61*</td>
</tr>
<tr>
<td></td>
<td>Employment status</td>
<td>−3.48</td>
<td>−2.20</td>
</tr>
<tr>
<td></td>
<td>Education level</td>
<td>0.04</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>Income level</td>
<td>4.05</td>
<td>3.38*</td>
</tr>
<tr>
<td></td>
<td>Cancer history</td>
<td>0.12</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>Intervention group</td>
<td>−1.37</td>
<td>−1.44</td>
</tr>
<tr>
<td>Genetic Testing Concerns</td>
<td>Baseline genetic testing</td>
<td>0.71</td>
<td>14.12*</td>
</tr>
<tr>
<td></td>
<td>concerns</td>
<td>−7.22</td>
<td>−3.12‡</td>
</tr>
<tr>
<td></td>
<td>Employment status</td>
<td>−1.17</td>
<td>−0.56</td>
</tr>
<tr>
<td></td>
<td>Education level</td>
<td>−0.82</td>
<td>−0.39</td>
</tr>
<tr>
<td></td>
<td>Income level</td>
<td>0.88</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>Cancer history</td>
<td>−3.53</td>
<td>−2.18†</td>
</tr>
</tbody>
</table>

NOTE: Employment status, employed versus not employed; education level, ≥ college versus < college; income level, <$75,000 versus ≥$75,000; cancer history: affected versus unaffected; intervention, PTC versus SGC. Because of a small amount of missing data for outcome variables and the income variable (<5%), not all models have the same sample size indicated above.

*P < 0.001.
†P < 0.05.
‡P < 0.01.

Discussion

A small but growing literature suggests that BRCA1/2 carriers may benefit from postdisclosure interventions over the short to intermediate term (17, 29). The current randomized controlled trial evaluated the effects of
Postdisclosure PTC on psychological functioning in female BRCA1/2 mutation carriers. Six months after result notification, BRCA1/2 mutation carriers randomized to PTC reported significant decreases in depressive symptoms, were less likely to meet criteria for clinically significant anxiety, and reported significant decreases in genetic testing distress relative to those randomized to SGC. To our knowledge, this is the first study to report that postdisclosure telephone counseling reduces short-term psychological distress among BRCA1/2 mutation carriers.

Although the beneficial effects of the PTC intervention were seen at 6 months but not at 12 months, there is reason to speculate that reducing distress in the immediate aftermath of receiving a positive test result could have important benefits. Considerable evidence documents the impact of affect on decision making and risk comprehension (10, 30, 31). Given the complexity of decision making following BRCA1/2 testing (32), an intervention that reduces distress during this crucial decision making period could improve informed decision making, risk comprehension, and family communication. Although PTC did not affect participants’ stress or confidence appraisals, future research should further explore the overall role of affect on BRCA1/2 risk management decision making (9–11).

In addition to the potential benefits on risk management decision making, our results and prior research suggest that adjunct interventions may provide benefits to subgroups of women who undergo BRCA1/2 genetic counseling and testing (9). Specifically, support programs such as PTC may be most useful for women identified by genetic counselors as highly anxious or undecided about management options (8). Future studies can explore the best methods for identifying such at-risk subgroups, investigate the theoretical mechanisms by which support programs produce change, and evaluate the most effective timing and delivery approaches for supportive adjunct interventions.

The short-term beneficial effect of PTC on depressive symptoms, clinical levels of anxiety, and genetic testing distress should be interpreted in a larger context. First, it is noteworthy that a telephone counseling intervention can have a positive effect on psychological functioning within this specific population. This novel method of care delivery increases the portability of counseling services by overcoming transportation and geographic barriers (33). Second, it is possible that reduced anxiety and distress may improve comprehension of genetic risk information and may facilitate decision making about screening, managing risk, and communicating risk information (31, 34). Third, it is important to note that although clinically relevant levels of anxiety were reduced, the level of depressive symptoms reported by participants would not require psychiatric intervention (24), findings consistent with prior research in this area (2). Although psychiatric intervention is not indicated for the majority of BRCA1/2 mutation carriers, interventions that provide short-term support may be beneficial for subgroups of carriers or women who self-select into these types of support interventions.

There are several limitations to this study. First, the small sample of 90 BRCA1/2 mutation carriers was homogeneous; participants were Caucasian and reported high levels of education and income. Results need to be evaluated using larger and more diverse samples to improve power to detect intervention effects and extend generalizability of the results. Second, not all PTC participants completed the intervention and we did not assess the extent to which the women read or used the intervention materials. These concerns are mitigated by our use of intention-to-treat analyses, the fact that the majority (76%) of women randomized to PTC did complete the intervention, and similar rates of study retention between the PTC and SGC groups. Third, the effect of the intervention observed at 6 months was not sustained at 12 months. Future work can explore the best methods to maintain long-term effects. Despite these limitations, the present study is the first randomized clinical trial to show the beneficial effects of postdisclosure telephone counseling on psychological functioning among mutation carriers. Given the availability of direct-to-consumer genetic testing for a variety of health conditions including online testing for the three BRCA1/2 founder mutations (35), the value of adjunctive support services such as PTC is likely to increase. Our findings add to the growing literature on adjunct interventions following genetic counseling by showing that a postdisclosure telephone psychosocial intervention is feasible and provides short-term benefits for BRCA1/2 carriers.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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