original article

Who is prone to high levels of distress after prophylactic mastectomy and/or salpingo-ovariectomy?

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Background: The present study aimed to assess predictors of distress after prophylactic mastectomy (PM) and salpingo-ovariectomy (PSO), in order to enable the early identification of patients who could benefit from psychological support.

Patients and methods: General distress and cancer-related distress were assessed in 82 women at increased risk of hereditary breast and/or ovarian cancer undergoing PM and/or PSO, before and 6 and 12 months after prophylactic surgery. Neurotic lability and coping were assessed before surgery.

Results: Cancer-related distress and general distress at both follow-up moments were best explained by the level of cancer-related and general distress at baseline. Being a mutation carrier was predictive of increased cancer-related distress at 6-month follow-up (but not at 12 months), and of lower general distress 12 months after prophylactic surgery. Also, coping by having comforting thoughts was predictive of less cancer-related distress at 6-month follow-up.

Conclusions: Genetically predisposed women who are at risk of post-surgical distress can be identified using one or more of the predictors found in this study. Exploration of and/or attention to cancer-related distress and coping style before prophylactic surgery may help physicians and psychosocial workers to identify women who might benefit from additional post-surgical support.

Key words: BRCA1/2, mastectomy, salpingo-ovariectomy, prophylactic surgery, psychology

introduction

Germline mutations in BRCA1 and BRCA2 account for approximately 3–5% of all breast and ovarian cancers. Women with a BRCA1/2 mutation have a significantly increased cumulative lifetime risk for breast cancer of 39–85%, and for ovarian cancer of 10–63% [1–3]. Furthermore, for mutation carriers with a history of breast cancer, the lifetime risk of developing a contralateral breast cancer is 35–64% [4]. The majority of families with a significant aggregation of breast/ovarian cancer remain genetically unidentified. Women from these families remain at increased risk of developing breast and/or ovarian cancer. Their lifetime risk is less clear but lower than for mutation carriers.

For both groups management options are either regular surveillance of the breasts and ovaries, or (bilateral) prophylactic mastectomy (PM or BPM), and/or prophylactic (bilateral) salpingo-ovariectomy (PSO or PBSO). Both prophylactic procedures result in a substantial risk reduction with respect to the occurrence of primary breast and ovarian cancer, respectively [3, 5–9].

Favourable effects of PM and/or PBSO on a woman’s distress level in the year following these interventions have been reported [10–17]. In mostly retrospective studies, post-surgical distress was related to surgical complications [18], psychiatric history, perceived risk of breast cancer [14], level of cancer-related distress at baseline, having children under the age of 15 years, less open communication of cancer issues within the family, having doubts about the genetic test outcome and changes in relationships with relatives [19]. No data are available on factors that are possibly predisposing for persisting increased distress in this group of women. Previously, we published results of a prospective study of women who opted for PM and/or PBSO with respect to the levels and course of distress after prophylactic surgery [20]. We found that anxiety and cancer-related distress were clearly diminished up to 1 year after prophylactic surgery. However, a subgroup

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remained with clinically significant levels of anxiety and
cancer-related distress. In the present analysis, we investigated
factors that might be predictive for increased distress at 6
months and 12 months after prophylactic surgery.

**patients and methods**

**patients**

At our family cancer clinic, prophylactic surgery consisting of either PM,
PBSO or both is discussed with mutation carriers and sometimes with
women from hereditary breast (and/or ovarian) cancer (HBC or HBOC)
families without an identified mutation. Women opting for either PM and/
or PBSO were invited to participate in a psychological follow-up study.

Previously unaffected women with a clinical diagnosis or suspicion of
cancer before prophylactic surgery were not eligible for participation. In
women with a history of breast cancer, absence of recurrent disease before surgery
was established by dissemination examination (chest X-ray, liver ultrasound, bone scan, liver functions and determination of Ca15.3/Ca125).
The institutional review board approved of the study.

**procedure**

After giving written consent, patients completed the first questionnaire
a week before surgery. This questionnaire contained questions on
demographic data, general and cancer-related distress, coping and
neuroticism. The second and third questionnaires, containing the outcome
measures, were completed 6 and 12 months after surgery.

**measures**

**independent variables**

**biographical and medical history information.** Data were
obtained on age, marital status, offspring, educational level and
profession, religious involvement and also carrier status, history
of breast/or ovarian cancer and type of prophylactic surgery.

**neuroticism.** The neuroticism (N-) scale of the Amsterdam
Biographical Questionnaire (ABQ) [21] assessed vulnerability
to experience psychological distress [22]. The subscale contains
30 items. Reliability for the neuroticism subscale in men and
women between the ages of 20 and 59 has been proven to be
good (0.95 and 0.84 respectively) [21].

**coping.** Coping was assessed using the Utrecht Coping List
(UCL) [23]. This instrument contains 47 items divided into
seven scales: Active Coping (i.e. taking action to solve
a problem), Palliative Reaction (i.e. seeking distraction),
Avoidance, Social Support Seeking, Passive Reaction (i.e. not
taking or not feeling able to take action), Expression of
Emotions and reassuring oneself by having Comforting
Thoughts. The scales are sufficiently consistent and
independent, and cover most areas of coping. Their validity
and reliability have been found to be good [24].

**outcome measures**

**cancer-related distress.** Cancer-related distress was assessed with
the Impact of Event Scale (IES) [25, 26]. The scale has been
used extensively in studies on adjustment to genetic
susceptibility testing and has satisfactory psychometric
properties. The IES measures intrusive and avoidant thoughts,
feelings and behaviour related to breast and/or ovarian cancer.
The score range for the total scale is 0 to 75.

**general distress.** General distress was measured with the
Hospital Anxiety and Depression Scale (HADS) [27]. The
HADS consists of two scales for anxiety and depression
respectively. The scores range from 0 to 21 for both scales. The
total scale of the HADS has been widely used as a screening
instrument in samples with minor psychiatric disorders.
Validity and reliability have been proven to be sufficient [28].

**statistical analysis**

The data were analysed using the SPSS 11.0 statistical package
(SPSS Inc., Chicago). Missing values were estimated using the
multiple imputation method. Significant differences on
biographical variables (i.e. age, level of education, marital
status, employment, children and religious involvement) and
medical variables (i.e. carrier status, type of surgery and history
of breast cancer) between participants and ‘drop-outs’ (see
later) were determined through Pearson’s $\chi^2$ tests.

Data were analysed through an elimination process by
performing multiple linear regression in the MPlus
3.1 program. All possible predictive variables (i.e. demographic
variables, neuroticism, coping and mean baseline scores on
general and cancer-related distress) were tested for their
predictive quality per measure of distress and time of
follow-up. The predictive variables ‘carrier status’ and ‘history
of breast cancer’ were dichotomized (mutation carriers or
women with a history of breast cancer were assigned a score of
1; risk carriers or women without a history of breast cancer
were assigned a score of 0).

The variables were categorized into candidate predictor
variables on the four outcome variables (cancer-related and
general distress at 6 and 12 months after prophylactic surgery).
Candidate predictor variables were only eligible if the
regression coefficient was significant at the 0.20 level of
significance, and eliminated if the regression coefficient
$P$ exceeded 0.25. The candidate predictor variables meeting the
eligibility criteria were entered simultaneously into the
regression model. Finally, the candidate predictor variables that
were significant contributors ($P = 0.05$) in estimating the
outcome were maintained in the final model. Variables were
eliminated from the analysis if the relevant unstandardized
regression coefficients were insignificant at the 0.05 level of
significance.

To gain insight into the robustness of the instrument, the
quality of the prognostic instrument (i.e. the ‘performance’
of the instrument) was measured by 10-fold cross-validation.

Parameters for the individual variables were the
unstandardized regression coefficient ($B$), the standardized
regression coefficient ($\beta$) and the standard error of the
unstandardized regression coefficient ($B$/standard error). As
measures of overall performance, $R^2$ was used in case of
continuous outcome variables. $R^2$ adjusted indicates the
adjustment for shrinkage.

**results**

**sample characteristics**

Between August 1999 and January 2003, 100 out of 129 eligible
women enrolled in the study (78%). Two women were
excluded because breast cancer was diagnosed between enrolment and PM. Further, the data of 16 women (drop-outs) filling out fewer than 75% of all items in the three questionnaires were excluded from the analysis. Accordingly, the final study group included 82 women. The study group and the drop-out group were not significantly different with respect to most biographical and medical data (Table 1).

The mean age at the time of PM and/or PBSO was 43 years. Most women in our study had a relationship with a partner (89%) and children (83%). The majority of both participants and drop-outs reported having a job (69% and 82% respectively). A quarter of the participants in the final study sample had finished higher education (vocational training or university) and 40% reported having an active religious involvement. Most women were mutation carriers (71% and 80% respectively), a history of breast cancer had occurred in 37% and 31% respectively and the majority (77% and 74% respectively) had opted for PM.

Coping strategies and neuroticism scores at baseline (Table 2) were compared with those of control women from the same age group. Mean scores of the participants in our study were in the average range [21, 24].

Table 3 shows the levels of general and cancer-related distress before surgery (T0) and at 6 months (T1) and 12 months (T2) after surgery. The decrease in general and cancer-related distress after prophylactic surgery was quadratically significant (\( P = 0.000 \) for both) [20].

**Table 1.** Characteristics of the women opting for prophylactic surgery (study sample and 16 drop-outs)*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Participants (( n = 82 ))</th>
<th>Drop-outs (( n = 16 ))</th>
<th>( df )</th>
<th>( F )</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>43 (±8.6) ( \text{M (SD)} )</td>
<td>43 (±8.9) ( \text{M (SD)} )</td>
<td>96</td>
<td>0.22</td>
<td>0.97</td>
</tr>
<tr>
<td>Marital status</td>
<td>Married or cohabiting</td>
<td>73 (89) ( \text{n (%)} )</td>
<td>13 (81)</td>
<td>3</td>
<td>6.44</td>
</tr>
<tr>
<td></td>
<td>Single or divorced</td>
<td>9 (11) ( \text{n (%)} )</td>
<td>3 (19)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children</td>
<td>Yes</td>
<td>68 (83) ( \text{n (%)} )</td>
<td>11 (73)</td>
<td>1</td>
<td>0.77</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>14 (17) ( \text{n (%)} )</td>
<td>4 (27)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Religious involvement</td>
<td>Low/average</td>
<td>61 (75) ( \text{n (%)} )</td>
<td>20 (25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>High</td>
<td>25 (31) ( \text{n (%)} )</td>
<td>9 (82)</td>
<td>1</td>
<td>0.79</td>
</tr>
<tr>
<td>Current job</td>
<td>Yes</td>
<td>55 (69) ( \text{n (%)} )</td>
<td>25 (31)</td>
<td>2</td>
<td>1.51</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>20 (25) ( \text{n (%)} )</td>
<td>10 (80)</td>
<td>4</td>
<td>5.23</td>
</tr>
<tr>
<td>Carrier status</td>
<td>BRCA1/2 mutation</td>
<td>58 (71) ( \text{n (%)} )</td>
<td>12 (80)</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>50% risk carrier</td>
<td>24 (29) ( \text{n (%)} )</td>
<td>3 (20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous cancer</td>
<td>No</td>
<td>52 (63) ( \text{n (%)} )</td>
<td>10 (63)</td>
<td>2</td>
<td>5.23</td>
</tr>
<tr>
<td></td>
<td>Breast cancer</td>
<td>30 (37) ( \text{n (%)} )</td>
<td>5 (31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ovarian cancer</td>
<td>0 (0) ( \text{n (%)} )</td>
<td>1 (6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of prophylactic surgery</td>
<td>PM</td>
<td>34 (42) ( \text{n (%)} )</td>
<td>4 (27)</td>
<td>4</td>
<td>1.64</td>
</tr>
<tr>
<td></td>
<td>P(B)SO</td>
<td>19 (23) ( \text{n (%)} )</td>
<td>4 (27)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PM + P(B)SO</td>
<td>9 (11) ( \text{n (%)} )</td>
<td>3 (20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PM before P(B)SO</td>
<td>5 (6) ( \text{n (%)} )</td>
<td>1 (7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>PM after P(B)SO</td>
<td>15 (18) ( \text{n (%)} )</td>
<td>3 (20)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Numbers deviating from \( n = 82 \) or \( n = 16 \) respectively indicate missing data.

PM + P(B)SO, prophylactic mastectomy and salpingo-oophorectomy simultaneously performed; PM before/after P(B)SO, prophylactic mastectomy performed before/after oophorectomy (time elapsed undefined).
cross-validation are similar, indicating that the findings are robust. General distress at 12-month follow-up had the highest $R^2 (0.42)$.

**Discussion**

To our knowledge, this is the first study to prospectively investigate predictors of distress after PM and/or P(B)SO in women opting for this type of surgery because of an increased risk of hereditary breast and/or ovarian cancer. The follow-up period extended up to one year after prophylactic surgery. In general, cancer-specific and general distress significantly decreased after prophylactic surgery [20]. However, increased levels of general and cancer-related distress at both 6 and 12 months after prophylactic surgery were found to be predicted by their respective baseline levels.

Consistent with previous findings [17, 20] we observed a decline of general and cancer-related distress after surgery. Although we do not have any quantitative data on additional counselling in other echelons of health care, the observed alleviation of distress could be related to post-operative counselling.

However, it appears that women who experienced high distress levels prior to prophylactic surgery tended to continue to experience high distress scores after prophylactic surgery. Possibly, their distress is not only related to the event of undergoing prophylactic surgery or the increased risk of developing cancer, but also to other factors, such as specific personality traits, coping strategies or life circumstances. In addition, they need to learn to live with the possible (physical) consequences of surgery.

Reassurance by having comforting thoughts proved to be in this study a favourable coping strategy at 6 months after prophylactic mastectomy/salpingo-ovariectomy, which was also observed in our study of women at increased risk for breast cancer adhering to surveillance [29]. No information is available on the contents of the comforting thoughts, and more research is needed before such a coping strategy could be facilitated or offered to specific women in clinical practice. For example, clinical experience has shown that women with young children are highly motivated to opt for far-reaching strategies in order to see their children grow up, which motivation might serve as a comforting or reassuring thought.

The role of mutation carrier status as a predictive factor was more difficult to interpret. Mutation carriers seem to benefit more after 12 months with regard to lower general distress than 50% risk carriers. However, at 6-month follow-up women opting for this type of surgery because of an increased risk of hereditary breast and/or ovarian cancer.
mutation carriers experienced more cancer-related distress, which fortunately was not found at 12 months. From previous studies it is known that mutation carriers opting for PM experience higher distress levels than those opting for surveillance, which is probably influenced by several factors (more or longer awareness of the genetic cancer susceptibility in the family, younger age and greater probability of having young children) [16, 30]. It may be possible that our observation reflects the vulnerability of the group of mutation carriers opting for PM, possibly influenced by personality traits, which is not altered by surgery over a short follow-up period. Certainly, it remains warranted to further address and explore this issue in future studies.

The uptake of prophylactic surgery in the Netherlands is quite high amongst mutation carriers compared with other Western countries [8, 31]. However, it also supports our clinical impression that women make their decisions while they are well-informed and do not base them on forms of maladaptive coping. Our results are relevant in helping to decide which patients might benefit from additional psychological counselling. Further research is warranted to elucidate the factors underlying continuous high levels of distress and to evaluate possibilities for therapeutic intervention.

This study underlines that a subgroup of women continues to show signs of mild psychological distress, even after prophylactic surgery. Given that prophylactic surgery is becoming a relevant risk-reducing management option that can be performed in many different ways (e.g. skin-sparing mastectomy, Transverse Rectus Abdominis Muscle flap procedure, Deep Inferior Epigastric Perforator flap procedure) depending on a woman’s preference, there is a strong need for further studies in this field.

references