Disclosure pattern and follow-up after the molecular diagnosis of BRCA/CHEK2 mutations

Journal of genetic counseling - ISSN 1059-7700 - 23:2(2014), p. 254-261
DOI: http://dx.doi.org/doi:10.1007/s10897-013-9656-5
Handle: http://hdl.handle.net/10067/1226470151162165141

J Genet Counsel
DOI 10.1007/s10897-013-9656-5

ORIGINAL RESEARCH

Disclosure Pattern and Follow-Up After the Molecular Diagnosis of BRCA/CHEK2 Mutations

D. Kegelaers · W. Merckx · P. Odeurs · J. van den Ende · B. Blaumeiser

Received: 2 June 2012 / Accepted: 5 September 2013

Abstract Five to 10 % of all breast cancer cases are due to mutations of high penetrance susceptibility genes, especially *BRCA1* and *BRCA2*. In families with known *BRCA* mutations, disclosure of genetic test results could induce relatives to undergo genetic testing themselves and adopt cancer risk management strategies, if necessary. This study examines disclosure patterns of individuals tested for mutations in the *BRCA1*, *BRCA2* and *CHEK2* genes to first-degree relatives with emphasis on a possible gender difference. It also assesses which management strategy is preferred by mutation-positive women in Belgium and the influence of psychological characteristics on communication and choice of management strategy. Ninety-nine adults from *BRCA/CHEK2* families, selected from the Centre of Medical Genetics of Antwerp, were included in the study. They were provided with medical and psychological questionnaires, the latter being the Self-Assessment Questionnaire, which is the Dutch version of the Spielberger State-Trait Anxiety Inventory and the Dutch version of the Coping Inventory for Stressful Situations (CISS-NL). The survey focused on disclosure, coping and management strategies with special attention on possible gender differences. The influence of socio-demographic and medical data on disclosure and cancer risk management as well as the influence of psychological features were examined by means of various statistical analyses. Ninety-nine patients were included, of whom 25 (25 %) were male. Eighty-seven percent of the participants informed all of their adult first-degree relatives about their mutation status without any gender discrimination. Seventy-eight percent of highly-educated participants informed all of their adult first-degree relatives, compared to 98 % of less formally-educated participants ($p=0.006$). The majority of mutation-positive women preferred prophylactic surgery to surveillance. Psychological differences appeared to have little influence on disclosure patterns and management strategies. The gender difference seems to be less pronounced than previously assumed. A striking observation, however, is the fact that significantly more participants who were less formally-educated informed all of their adult first-degree relatives, compared to participants who were highly-educated. In our study population, most female mutation carriers opted for prophylactic surgery. Since the study population is small, further studies are needed to enhance the generalizability of these results.

Keywords BRCA · Genetic counseling · Gender difference · Disclosure · Prophylactic surgery

Introduction

The detection of *BRCA* genetic mutations in familial clustering of breast and ovarian cancers constitutes a key role in estimating the cancer risk. In a study by Ford et al. (1998) the contribution of *BRCA1* and *BRCA2* to inherited breast cancer was assessed by linkage and mutation analysis in 237 families, each with at least four cases of breast cancer. Families were included without regard to the occurrence of ovarian or other cancers. Overall, disease was linked to *BRCA1* in 52 % of families, to *BRCA2* in 32 % of families, and to neither gene in 16 %, suggesting other predisposition genes. The majority (81 %) of the breast-ovarian cancer families were due to

D. Kegelaers, W. Merckx and P. Odeurs contributed equally to the article.

D. Kegelaers · W. Merckx · P. Odeurs · J. van den Ende · B. Blaumeiser (✉)
Department of Medical Genetics, University and University Hospital of Antwerp, Prins Boudewijnlaan 43, 2650 Edegem, Belgium
e-mail: bettina.blaumeiser@ua.ac.be

D. Kegelaers · B. Blaumeiser
Gynecology and Obstetrics, University Hospital of Antwerp, Edegem, Belgium

Published online: 11 October 2013

BRCA1. Conversely, the majority of families with male and female breast cancer were due to *BRCA2* (76 %).

The Anglian Breast Cancer Study Group (2000) screened a population-based series of 1,220 breast cancer cases diagnosed before the age of 55 for mutations in *BRCA1* and *BRCA2*. Breast cancer penetrance by age 80 was estimated to be 48 % (95 % CI 7–82 %) for *BRCA1* mutation carriers and 74 % (7–94 %) for *BRCA2* mutation carriers. Ovarian cancer penetrance by age 80 was 47 % (5–100 %) for *BRCA1* mutation carriers and 14 % (2–68 %) for *BRCA2* mutation carriers. The *CHEK2* Breast Cancer Case–Control Consortium (2004) evaluated the association between CHEK2*1100delC and breast cancer risk at the population level. A total of 10,860 breast cancer cases and 9,065 controls from 10 case–control studies in five countries were genotyped. *CHEK2**1100delC was found in 201 cases (1.9 %) and 64 controls (0.7 %) (estimated odds ratio 2.34; 95 % CI 1.72–3.20; $P = .0000001$).

To individuals with a known family history of *BRCA/CHEK2*-related cancers *BRCA/CHEK2* mutation testing can be offered. In case of a positive test (i.e. identification of a pathogenic mutation), several measures can be taken to manage the risk of cancer. Risk management strategies for women with a mutation in *BRCA1* or *BRCA2* include risk reducing surgery (mastectomy and/or salpingo-oophorectomy), chemoprevention or cancer screening (clinical breast examination, mammography, breast ultrasound, breast MRI, trans-vaginal ultrasound and CA-125 examination) (Nelson et al. 2005).

Bilateral prophylactic mastectomy and bilateral prophylactic salpingo-oophorectomy decrease the risk of breast and ovarian cancer in *BRCA* mutation carriers (Hartmann et al. 2001; Kauff et al. 2002). The effect of chemoprevention in this group is still uncertain (King et al. 2001). Breast cancer screening using mammography, ultrasound and magnetic resonance imaging can detect breast cancers with favorable prognostic characteristics (Warner et al. 2004). The benefits of ovarian cancer screening in high-risk populations are less clear (Hogg and Friedlander 2004).

The prospective studies by Phillips et al. (2006) and van Dijk et al. (2008) show that the majority of mutation carriers choose the least invasive management strategy. Van Dijk et al. (2008) describe that women having young children (i.e., younger than age 13 years) and women with a personal history of breast cancer are more likely to prefer prophylactic mastectomy. Among the women with a history of breast cancer, those having undergone a unilateral radical mastectomy are more in favor of having a contralateral prophylactic mastectomy. Also women who show higher levels of state anxiety according to the "Spielberger State-Trait Anxiety Inventory" are more inclined to undergo preventive surgery.

As genes causing hereditary breast and ovarian cancers are passed on in an autosomal dominant pattern, *BRCA* carriers have a major responsibility towards family members. The findings of Finlay et al. (2008) show that the majority of *BRCA* carriers share the results of their tests with all of their family members at risk and that all of them disclose the result to at least one family member at risk. First-degree relatives are more often informed than second- or third-degree relatives. This is confirmed by MacDonald et al. (2007), McKinnon et al. (2007) and Wagner Costalas et al. (2003).

The study by Finlay et al. (2008) shows that approximately as many male as female relatives are informed, but other studies (MacDonald et al. 2007; Patenaude et al. 2006; Wagner Costalas et al. 2003) show that mainly female relatives are informed. Whereas the study by Finlay et al. also includes male *BRCA* mutation carriers in its study population, this is not the case in other studies. Can we therefore conclude that female carriers mainly inform women of their *BRCA* status and that male carriers mainly inform men?

Few studies on the subject of mutation disclosure also involve male mutation carriers in their study population. As a result, very little is yet known about the differences in communication between men and women. The purpose of our study was to obtain a better insight into and understanding of communication patterns used by male and female carriers when informing their adult first-degree relatives about their test results, in order to improve the genetic counseling of these carriers. Gender was the main factor studied in this report to show the difference in communication of *BRCA* carriers with their relatives; other factors such as age and cancer state, which might have an influence on communication, were also included. The study also investigated which management strategies were preferred by *BRCA/CHEK2*-positive women in Belgium. Factors which may influence the choice for prophylactic surgery are also examined, and whether the results were compatible with findings from previous studies in different populations. Finally, we considered the influence of some psychological characteristics such as anxiety and coping strategy on communication and choice of management strategy.

Methods

Study Group

The population involved in this study has been selected from the databank of the CMG Antwerp (Centre of Medical Genetics of the University and University Hospital of Antwerp). Criteria for inclusion were a prior *BRCA/CHEK2* mutation analysis and to be a member of a *BRCA/CHEK2* family (i.e. that at least one family member has to be carrier of a mutation in one of the above genes). All participants whether testing positive or negative in the DNA test were included in the study. An additional

condition was that the selected people underwent genetic molecular diagnosis before 1 January 2009. The participants needed to have had sufficient time to obtain information about their condition and the possibility to have themselves treated with the most suitable management strategy. A criterion for exclusion was that the detected mutation was a UV (unclassified variant), which means that the pathogenicity of the mutation had not been proven at the time of the test.

The ethic committee of the University Hospital of Antwerp reviewed our study design and gave their approval. Afterwards, a letter was sent to the selected patients. This letter enclosed an explanation about the study, as well as a registration form by which they could indicate if they wanted to participate in the study. The letter also included an invitation to a *BRCA/CHEK2* symposium. Selected patients who did not send their registration form back, got a phone call from the investigators to inquire if they were interested to participate in the study. Two weeks before the symposium, participants got a reminder. The symposium was held on February 20, 2010. Several experts from different medical branches (gynecology, oncology, genetics, plastic surgery and psychology) were invited to speak about BRCA/CHEK2 related topics, followed by the testimony of a BRCA patient, who was also chairwoman of the Belgian self-support group for BRCA patients "Natarelle." After this testimony, patients were invited to complete medical and psychological questionnaires. Patients who wanted to participate in our study, but could not be present at the symposium, got a new information letter as well as the psychological questionnaires. Participants who completed and returned their questionnaires got a phone call from the authors to complete the medical questionnaire.

Instrumentation

The medical questionnaire was prepared and completed by the investigators themselves to retrospectively assess socio-demographic, medical and communicative data and to avoid reporting bias. Socio-demographic data including personal data (gender, age, marital status, GPA, highest qualification attained and occupation) and the ethnicity of the four grandparents together with a pedigree were noted. Regarding the medical field, for participants without a personal history of cancer, *BRCA* status and management strategy were included. For participants with a personal history of cancer, their cancer diagnosis, the therapy and any recurrence were noted. Questions concerning communication were asked to establish which first-degree relative was informed first about the test results and what amount of time had elapsed after the molecular diagnosis, what other relatives had been informed and finally, whether or not children had been informed and what their ages were at that time.

Concerning the communication part, the study only takes adult first-degree relatives into account. Younger children are not always informed. Parents attribute this to their children's still low level of understanding about inheritance and risk of cancer at a later stage of life. Furthermore the CMG Antwerp usually advises mutation carriers not to inform their children under the age of 18.

The researchers used two psychological questionnaires, namely the Self-Assessment Questionnaire (van der Ploeg 2000), which is the Dutch version of the Spielberger State-Trait Anxiety Inventory (Spielberger et al. 1983) and the Dutch version of the Coping Inventory for Stressful Situations (CISS-NL) (Endler and Parker 1990; de Ridder and van Heck 1999).

The Spielberger State-Trait Anxiety Inventory (Cronbach's alpha reliability coefficient >0.90) principally measures two types of anxiety: state anxiety and trait anxiety. The researchers were specifically interested in trait anxiety. This refers to relatively stable individual differences in anxiety sensitivity (van der Ploeg 2000).

Twenty questions were scored using a 4-point scale, where a minimum of 20 (very low anxiety) and a maximum of 80 (very high anxiety) could be achieved.

The Coping Inventory for Stressful Situations (Cronbach's alpha >0.80) measures coping styles: the participants are asked how they usually deal with stressful situations. Three coping styles are to be distinguished: task-oriented coping (i.e. solving or cognitive restructuring of the problem or changing the situation), emotion-focused coping (i.e. emotional responses which aim to reduce stress) and avoidance-oriented coping (which can be directed towards the stressor or towards the feelings evoked by the stressor). Avoidance-oriented coping can furthermore be divided into "searching for distraction" and "searching for companionship" (de Ridder and van Heck 1999). There were 16 questions for each coping style which were scored using a 5-point scale. Scores for each coping style therefore could range from 16 to 80, with higher scores indicating a stronger tendency towards using that style.

Data Analysis

SPSS 17.0 was used to analyze the data. The study population was characterized by means of descriptive statistics. The influence of socio-demographic and medical data on communication patterns and the choice of cancer risk management strategy, was analyzed using Pearson's chi-square test or, when the number of observations in the group was too small, by means of a two-sided Fisher's exact test. Management strategies were visualized by means of bar charts. The influence of trait anxiety on communication and management strategy was demonstrated using the *t*-test and the influence of coping was shown using

binary logistic regression. Normality was checked by means of the Kolmogorov–Smirnov test.

Results

Participants

Of 255 selected participants, 79 agreed to attend our symposium and participate in this study, 61 were willing to participate in our study, but could not make it to the symposium, and 115 were not interested at all or could not be reached. Of the 79 participants that were present at our symposium, 54 filled in both questionnaires. Seven people were present, but did not complete all the questionnaires. Five of them filled in the psychological questionnaires. All 5 completed their medical questionnaire during a phone call with one of the investigators. Two participants filled in their medical questionnaire at the symposium, but the investigators never received their psychological questionnaires. Eighteen participants didn't fill in any of the questionnaires. Of the 61 people who did not attend the symposium but were willing to participate in the study, 41 filled in the psychological questionnaires. Forty of them could also be contacted by telephone to complete their medical questionnaires.

Ninety-nine patients, aged 19–79 years (mean=49 years), were included in the study (54 symposium attendees that filled in both questionnaires, 5 symposium attendees that filled in the psychological questionnaires and completed their medical questionnaire by phone, 40 non-attendees). The majority of the patients were female (75 %), married (74 %), with children (81 %) and highly-educated (57 %). Highly-educated participants had a bachelor's or master's degree, while less formally-educated participants had only obtained a primary- or secondary-education diploma (Belgian education structure). Sixty-six participants (67 %) were mutation-positive (19 *BRCA1*, 44 *BRCA2*, 3 *CHEK2*), and 71 participants (72 %) had no personal history of cancer. All patients were either from Caucasian or Ashkenazi-Jewish origin.

Communication

Two mutation-positive women, who had no living adult first-degree relatives, were not involved in the communication part of the study. Eighty-seven percent (84/97) informed all of their adult first-degree relatives about their mutation status; 84 % (21/25) of male participants and 87 % (63/74) of female participants informed all of their adult first-degree relatives about their test results. There was no significant difference between male and female participants as to the number of informed first-degree relatives ($p=0.735$). Two participants informed none of their adult first-degree relatives. Ninety-five participants informed at least one first-degree relative about their mutation status. Ninety-four percent (89/95) informed their first first-degree relative on the same day they had heard about their test result. There was a significant gender difference in the celerity of information flow, as 97 % (68/74) of female participants and 84 % (21/25) of male participants did this the very same day ($p=0.04$).

Eighty-seven participants had both male and female living adult first-degree relatives at the time they were informed about their genetic status. Sixty-three percent (55/87) first informed a female first-degree relative, 18 % (16/87) first informed a male first-degree relative, and 18 % (16/87) communicated their test results to both sexes at the same time (e.g. to both of their parents). Significantly more female participants (85 %—44/52) than male participants (58 %—11/19) first informed a female first-degree relative ($p=0.017$). Ninety percent (78/87) of participants who had both male and female living first-degree relatives communicated their test results equally to both sexes without a significant gender difference [86 % (19/22) of male participants and 91 % (59/65) of female participants ($p=0.686$)].

Seventy-eight percent (44/56) of highly-educated participants and 98 % (40/41) of less formally-educated participants informed all of their adult first-degree relatives about their test results ($p=0.006$). This shows that the degree of education significantly influences communication patterns. It seems that highly-educated participants less frequently inform all of their adult first-degree relatives. Ninety-five percent (39/41) of less formally-educated participants and 93 % (50/54) of highly-educated participants informed their first first-degree relative on the same day the test results had been announced. There is no significant difference regarding the celerity with which their first first-degree relative was informed ($p=0.696$).

Eighty-eight percent (29/33) of mutation-negative participants and 86 % (55/64) of mutation-positive participants informed all of their adult first-degree relatives. So, there is no significant difference between carriers and non-carriers as to the number of first-degree relatives that they informed ($p=1.0$). Ninety-four percent (31/33) of mutation-negative and 95 % (58/62) of mutation-positive participants informed their first first-degree relative on the same day the result had been announced. So, there is no significant difference between carriers and non-carriers with regard to the lapse of time between learning the test result and informing their first first-degree relative ($p=1.0$).

Eighty-five percent (22/26) of mutation-positive women without a personal history of cancer and 89 % (23/26) of mutation-positive women with a personal history of cancer informed all of their adult first-degree relatives. There is no significant difference between mutation-positive women with and without a personal history of cancer with regard to the number of first-degree relatives that they informed ($p=1.0$). All mutation-positive women without a personal history of cancer and 92 % (24/26) of mutation-positive women with a

personal history of cancer announced the test results on the same day they had been informed about their genetic status. No significant difference based on cancer status can be observed in the celerity with which their first first-degree relatives were informed ($p=0.491$).

Risk Management Strategies Chosen by BRCA/CHEK2-Positive Women

Fifty-four of 99 participants were mutation-positive women. All of them had decided to take measures to reduce or follow their significantly increased breast and ovarian cancer risk and avoid possible health problems in the future. Seventy percent (38/54) had already undergone one or more preventive surgeries (mastectomy, salpingo-oophorectomy or both). The remaining 30 % (16/54) decided to have themselves regularly screened; most undergo a clinical examination of ovaries and breasts combined with an ultrasound of the ovaries each year and a mammography with an ultrasound of the breasts every 2 years. Some of them, especially those younger than 30, undergo a breast MRI every 2 years.

The average age of the women who had undergone preventive surgery is 46.6 years old. The average age of those who opted for screening only, is 45.3 years old. Regarding the choice of management strategy, there is no significant difference due to the age factor ($p=0.876$).

Seventy-four percent (20/27) of less formally-educated participants and 67 % (18/27) of highly-educated participants opted for preventive surgery. Educational achievement does not seem to affect the choice of management strategy ($p=0.551$).

Sixty-eight percent (19/28) of women without a personal history of cancer and 73 % (19/26) of women with a personal history of cancer have had preventive surgery. There is no significant difference between women with and without a personal history of cancer in the choice of management strategy ($p=0.675$).

Sixty-three percent (24/38) of mutation-positive women who opted for preventive surgery had their adnexa as well as their breasts removed. This number also includes the women who had already undergone this surgery for other reasons and who afterwards had their remaining *BRCA*-sensitive organs preventively removed. Twenty-six percent (10/38) had only their adnexa removed and 11 % (4/38) only their breasts.

Influence of Psychological Characteristics on Communication and Choice of Risk Management Strategy

The average trait anxiety of the 84 participants who informed all of their adult first-degree relatives, was 37.12. The average trait anxiety of the remaining 13 participants, who did not disclose their genetic status to all first-degree family members, was 39.77. Trait anxiety does not seem to influence the number of first-degree relatives that are informed about mutation status ($p=0.365$). The average trait anxiety of the 89 participants who informed their first first-degree relative on the day of hearing about their test results, was 37.35. For the remaining 6 participants, the score was 37.67. There is no significant difference based on trait anxiety in the celerity with which their first first-degree relative had been informed ($p=0.938$). The average trait anxiety of the 16 mutation-positive women who preferred not to undergo preventive surgery, was 38.00 and the score of the 38 other mutation-positive women who decided to have a preventive operation, was 38.87. There was no significant difference on the basis of fear in the choice of risk management strategy ($p=0.776$).

Concerning the influence of coping on whether or not to inform all first-degree relatives only emotion-focused coping has a significant influence ($p=0.02$). The more a person is prone to emotion-focused coping, the less likely this person will inform all of his or her first-degree relatives. There was no significant relationship in for task-oriented ($p=0.084$) or avoidance-oriented coping ($p=0.168$). The celerity with which the first first-degree relative was informed about the test results, was only significantly affected by avoidance-oriented coping ($p=0.046$). The more avoidance-oriented coping style one has, the greater the chance that one will inform a first-degree relative on the day of the molecular diagnosis. Analyses of task-oriented and emotion-oriented coping yielded respective p-values of 0.121 and 0.152. With *BRCA/CHEK2*-positive women, coping styles had no significant influence on whether or not to opt for preventive surgery. The *p*-values for task-, emotion- and avoidance-oriented coping were respectively 0.965, 0.960 and 0.913.

Discussion

Communication

This is the first Belgian study which analyzes the effect of gender on communication with first-degree relatives within *BRCA/CHEK2* families. This research shows that first-degree relatives are equally informed, regardless of their gender. This is consistent with the findings of Finlay et al. (2008) but contradicts Patenaude et al. (2006), MacDonald et al. (2007) and Wagner Costalas et al. (2003). Since the study of Finlay et al. (2008) tested both men and women for *BRCA* in their population but the other studies (MacDonald et al. 2007; Patenaude et al. 2006; Wagner Costalas et al. 2003) did not, the question was raised if one can conclude that female carriers disclose their results mostly to women and male carriers mostly to men? This seems not to be the case, so we can conclude that in our study population there is a thorough understanding of the importance of good communication with all family members. We believe that effective genetic counseling played a role in this increased communication. A small

minority, however, still has a preference to inform mainly women. It remains therefore important to give sufficient information during genetic counseling. Although most participants informed both sexes equally, it is clear that more female than male participants informed a female first-degree relative first about their mutation status. This could be explained by the fact that the first disclosure is emotionally the heaviest and that the involved person might feel better understood by someone of the same sex. The subsequent disclosures may be less emotionally difficult.

The only parameter that appears to have some influence on the number of first-degree relatives who have been informed is the level of education of the participant. It is noteworthy that highly-educated people seem less likely to disclose their test results to all of their first-degree relatives than less highly-educated people. This finding was not expected. One could assume that highly-educated people, who are better capable of assessing the severity of the problem and the necessity of genetic testing, would inform their first-degree relatives more often than the less formally-educated. One possible explanation is that highly-educated people have a better understanding of the impact that this information could have on especially elderly relatives and that they would want to spare them additional concerns. Another explanation might be found in family relationships. If highly-educated people have looser family ties than unskilled workers, they are less inclined to share their information. Further studies are needed to find out the actual cause behind these observations.

Women appeared more likely than men to inform their first first-degree relative on the same day of the molecular diagnosis. A possible explanation could be that men need more time to fully process the information for themselves, while women seek support from friends and family. Also, women may be more likely to have themselves accompanied by a family member when they go to a medical appointment. Another hypothesis is that men inform their first-degree relatives indirectly, for example through their partner or their sister. This could be further explored in subsequent studies. Apart from the gender factor, medical and socio-demographic data seem to have no influence on the lapse of time between knowing the test results and the transfer of related information to a first-degree relative.

Risk Management Strategies Chosen by BRCA/CHEK2-Positive Women

A striking observation is that all mutation-positive women reported using one of the available cancer risk management strategies. Within this population 70 % have opted for preventive surgery. This is inconsistent with the findings of Phillips et al. (2006) and van Dijk et al. (2008), who came to the conclusion that the majority of female carriers chose the least invasive management strategy. This study shows that preventive surgery may be more popular than screening in the Antwerp region. Because each individual with a positive *BRCA/CHEK2* mutation status carries a very high risk of developing cancer (Anglian Breast Cancer Study Group 2000; CHEK2 Breast Cancer Case–Control Consortium 2004), and surgery is the only strategy that significantly reduces the risk, this is considered a very positive development. It could be attributed to proper genetic counseling and gynecological risk management policy whereby each option is clearly explained. During genetic counseling patients were informed about pro's and con's of each preventive strategy, either intensive screening or prophylactic surgery. Genetic counselors did not make a decision for their patients, but gave them an open view of possible strategies to manage their BRCA/CHEK2 mutation. At the end of each counseling session, the decision for prophylaxis was made by the patients themselves and not by their attending physician. In addition, surgical procedures have been greatly improved and now provide better cosmesis. For instance, breast reconstruction with the patient's own tissue and nipple reconstruction have an excellent aesthetic result. An additional explanation of the fact that Flemish women often opt for preventive surgery could be found in the identity and character of this population group. It might be interesting to investigate ethnographic differences in future studies.

In our study younger women without a personal history of cancer less often opted for preventive surgery than older women without a personal history of cancer. This could be attributed to the fact that in view of their age they greatly value their body shape and their assumption that they can continue living for a number of years without any symptoms and that surgery is not urgent yet. Also they may still want to have children and they may feel too young to choose surgical menopause. If these women do decide to undergo prophylactic surgery, both adnexa and breasts are more often removed than in the case of women who are older than 40. The reason most likely is that once the young women have made this difficult decision, they will usually opt for the surgery that offers the best guarantee of disease-free survival. Women over the age of 40 often opt for salpingo-oophorectomy as they are already with children and are approaching or are already in menopause. Women over the age of 40 with a personal history of cancer more often opt for surgery that removes both adnexa and breasts, than women over the age of 40 without a personal history of cancer. Most of these women have already undergone surgical procedures, often because of breast cancer, and are therefore more willing to have their remaining *BRCA*-sensitive organs removed. Having already experienced the development of cancer, constitutes an extra motivation as well.

Influence of Psychological Characteristics on Communication and Choice of Risk Management Strategy

Concerning psychological characteristics, fear apparently has no effect on the number of first-degree relatives who are

informed, nor on the celerity with which this happens. Also on the choice between screening and preventive surgery anxiety seems to be of little influence. Most women opted for the most effective management strategy, namely surgery. Although Van Dijk et al. (2008) noticed that mainly anxious women opt for preventive surgery, anxiety seems to be substantially less influential than other factors such as anticipated feelings of regret.

Concerning coping strategies the number of first-degree relatives who are informed, is mainly determined by emotion-focused coping. The more emotion-focused coping one has, the greater the chance that one will not inform everybody. A possible explanation is that in case of problems, people with a tendency to engage on emotion-focused coping, are carried away by their feelings and blame themselves and others. Therefore they are less capable to share their test results with others. The celerity with which the first first-degree relative is informed, is mainly determined by avoidance-oriented coping. Someone with a tendency to avoidance-oriented coping, will sooner inform his or her first first-degree relative. This seems contradictory, but talking about their problems, helps people with a tendency to avoidance-oriented coping, to come to terms with the situation. Coping styles appear to have no influence on whether people opt for prophylactic surgery or not. Like anxiety, coping styles seem to be substantially less important in the process of decision making.

Limitations

Limitations of this study include the fact that our results are based on a small number of patients and therefore need to be replicated on a larger sample. In some cases the statistical power might be too low to detect a significant difference. In addition, our study potentially suffers from memory and sampling bias. As attendance at the symposium and participation in the study afterwards were strictly voluntary, a sampling bias cannot be thoroughly avoided. The fact that a majority of our female mutation participants pursued preventive surgery can easily be attributed to sampling bias rather than to the identity and character of our study population. The very high number of participants who had disclosed their mutation status to all of their first-degree relatives may also reflect sampling bias. The people who partook in the study may have had a better understanding of the importance of genetics. In that case they likely would have been more engaged to inform their relatives about their mutation status and to take proper risk management strategies.

Also memory bias may have affected our results. For a large part we had to rely on the memory of our participants, especially regarding the communicative aspect. For example, sometimes they did not easily remember which first-degree relative they informed first.

Despite these limitations, we consider our results noteworthy as they offer insights about male communication patterns as well as participants having a lower education level. Furthermore, future studies can be guided by the results regarding the disclosure in the less educated patient population.

Conclusion

This is the first study which analyzes the effect of gender on disclosure of genetic information within Belgian *BRCA/CHEK2* families. Our research shows that neither male nor female first-degree relatives are discriminated against when communicating genetic information and that both men and women inform all of their first-degree relatives within a reasonable lapse of time. Significantly more participants who were less formally-educated informed all of their adult first-degree relatives, compared to participants who were highly-educated. Contrary to what has already appeared in literature, female mutation carriers clearly opt more for the most effective cancer risk management strategy (i.e. surgery). Psychological characteristics proved to have less effect than we expected. As the population group is rather small and an ascertainment bias cannot be ruled out, further research on a larger population is required. It might also be interesting to conduct further studies into the influence of the degree of education on communication patterns, the communication of information to children and the influence of ethnographic differences on the choice of cancer risk management strategies.

References

Anglian Breast Cancer Study Group. (2000). Prevalence and penetrance of *BRCA1* and *BRCA2* mutations in a population-based series of breast cancer cases. *British Journal of Cancer, 83*(10), 1301–1308.

CHEK2 Breast Cancer Case–Control Consortium. (2004). *CHEK2** 1100delC and susceptibility to breast cancer: a collaborative analysis involving 10,860 breast cancer cases and 9,065 controls from 10 studies. *American Journal of Human Genetics, 74*(6), 1175–1182.

de Ridder, D. T. D., & van Heck, G. L. (1999). *Coping Inventory for Stressful Situations: Handleiding* (p. 15, 25, 26). Amsterdam: Pearson.

Endler, N. S., & Parker, J. D. A. (1990). *Coping Inventory for Stressful Situations (CISS): Manual*. Toronto: Multi-Health Systems.

Finlay, E., Stopfer, J. E., Burlingame, E., Goldfeder Evans, K., Nathanson, K. L., Weber, B. L., et al. (2008). Factors determining dissemination of results and uptake of genetic testing in families with known *BRCA1/2* mutations. *Genetic Testing, 12*, 81–92.

Ford, D., Easton, D. F., Stratton, M., Narod, S., Goldgar, D., Devilee, P., et al. (1998). Genetic heterogeneity and penetrance analysis of the *BRCA1* and *BRCA2* genes in breast cancer families. *American Journal of Human Genetics, 62*(3), 676–689.

Hartmann, L. C., Sellers, T. A., Schaid, D. J., Frank, T. S., Soderberg, C. L., Sitta, D. L., et al. (2001). Efficacy of bilateral prophylactic mastectomy in BRCA1 and BRCA2 gene mutation carriers. *Journal of the National Cancer Institute, 93*, 1633–1637.

Hogg, R., & Friedlander, M. (2004). Biology of epithelial ovarian cancer: implications for screening women at high genetic risk. *Journal of Clinical Oncology, 22*, 1315–1327.

Kauff, N. D., Satagopan, J. M., Robson, M. E., Scheuer, L., Hensley, M., Hudis, C. A., et al. (2002). Risk reducing salpingo-oophorectomy in women with a BRCA1or BRCA2 mutation. *New England Journal of Medicine, 346*, 1609–1615.

King, M. C., Wieand, S., Hale, K., Lee, M., Walsh, T., Owens, K., et al. (2001). Tamoxifen and breast cancer incidence among women with inherited mutations in BRCA1 and BRCA2. National Surgical Adjuvant Breast and Bowel Project (NSABP-P1) Breast Cancer Prevention Trial. *JAMA, 286*, 2251–2256.

MacDonald, D. J., Sarna, L., van Servellen, G., Bastani, R., Giger Newman, J., & Weitzel, J. N. (2007). Selection of family members for communication of cancer risk and barriers to this communication before and after genetic cancer risk assessment. *Genetics in Medicine, 9*, 275–282.

McKinnon, W., Naud, S., Ashikaga, T., Colletti, R., & Wood, M. (2007). Results of an intervention for individuals and families with *BRCA* mutations: a model for providing medical updates and psychosocial support following genetic testing. *Journal of Genetic Counseling, 16*, 433–456.

Nelson, H. D., Huffman, L. H., Fu, R., & Harris, E. L. (2005). Genetic risk assessment and BRCA mutation testing for breast and ovarian cancer susceptibility: systematic evidence review for the US preventive services task force. *Annals of Internal Medicine, 143*, 362–379.

Patenaude, A. F., Dorval, M., DiGianni, L. S., Schneider, K. A., Chittenden, A., & Garber, J. E. (2006). Sharing *BRCA1/2* test results with first-degree relatives: factors predicting who women tell. *Journal of Clinical Oncology, 24*, 700–706.

Phillips, K. A., Jenkins, M. A., Lindeman, G. J., McLachlan, S. A., McKinley, J. M., Weideman, P. C., et al. (2006). Risk-reducing surgery, screening and chemoprevention practices of *BRCA1* and *BRCA2* mutation carriers: a prospective cohort study. *Clinical Genetics, 70*, 198–206.

Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). *Manual for the State-Trait Anxiety Inventory*. Palo Alto: Consulting Psychologists Press.

van der Ploeg, H. M. (2000). *Handleiding bij de Zelf-Beoordelings Vragenlijst*. 2e ed (p. 5, 6, 27). Amsterdam: Pearson.

van Dijk, S., van Roosmalen, M. S., Otten, W., & Stalmeier, P. F. M. (2008). Decision making regarding prophylactic mastectomy: stability of preferences and the impact of anticipated feelings of regret. *Journal of Clinical Oncology, 26*, 2358–2363.

Wagner Costalas, J., Itzen, M., Malick, J., et al. (2003). Communication of *BRCA1* and *BRCA2* results to at-risk relatives: a cancer risk assessment program's experience. *American Journal of Medical Genetics Part C: Seminars in Medical Genetics, 119*, 11–18.

Warner, E., Plewes, D. B., Hill, K. A., Causer, P. A., Zubovits, J. T., Jong, R. A., et al. (2004). Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography and clinical breast examination. *JAMA, 292*, 1317–1325.