Chapter #2

PSYCHOLOGICAL DISTRESS AND COPING STRATEGIES AMONG WOMEN WHO UNDERGO CANCER GENETIC TESTING

Valentina Di Mattei[1,2], Martina Bernardi[1], Fabio Madeddu[3], & Lucio Sarno[1,2]
[1]*San Raffaele Hospital, Milan, Italy*
[2]*Vita Salute San Raffaele University, Milan, Italy*
[3]*Milano-Bicocca University, Milan, Italy*

ABSTRACT
Carriers of BRCA mutations (BRCA1 and BRCA2) have a higher risk for breast and ovarian cancer. Although cancer genetic testing is an effective instrument for cancer prevention, little is known about the psychological impact it may have on its users. The aim of the present study is to investigate the effect of coping strategies on the prediction of psychological distress among women who decide to undergo cancer genetic testing; distinguishing them by their reasons for undertaking genetic testing. The study included three groups of women: breast and/or ovarian cancer patients (N = 33), breast and/or ovarian cancer survivors (N = 22) and people with strong family histories for breast and/or ovarian cancer (N = 10). All cancer patients (both in/out of remission) were affected by breast or ovarian cancer. Assessment of psychological distress and coping strategies were respectively obtained with the administration of the SCL-90-R and the COPE-NVI questionnaires. ANOVA and multiple regression models were carried out. Groups of participants significantly differed with regards to somatization, depressive symptoms and hostility. The use of avoidance coping strategies predicted higher levels of psychological distress. Results from the present study suggest the importance of coping strategies on the prediction of psychological distress, allowing psychologists to draw up appropriate intervention strategies during cancer genetic testing.

Keywords: cancer, genetic counseling, cancer genetic testing, hostility, coping.

1. INTRODUCTION

In the field of genetic oncology, the clinical process that leads to the diagnosis of hereditary tumors and to the management of genetically high-risk subjects is called Cancer Genetic Counseling. Presently, it is estimated that 7-8% of breast cancers and 10% of ovarian cancers are hereditary forms of the disease (Vuttariello et al., 2013): the genetic basis of the Hereditary Breast and Ovarian Cancer (HBOC) syndrome is, in most cases, a germline inherited mutation in either the BRCA1 or BRCA2 genes (Vuttariello et al., 2013; Brédart et al., 2013), which are found respectively on chromosomes 17 and 13 (Miki et al., 1994; Wooster et al., 1995). A mutation of these oncosuppressors is usually an alteration or suppression of gene function (a loss of function), which leads to uncontrolled cellular proliferation and, as a consequence, a tumor develops. In these cases the mutation involves germline cells and is inherited as an autosomal dominant trait with incomplete penetration. Inheriting these germline alterations means a higher risk of developing breast or ovarian cancer compared to the general population, but this does not equate to certainty of disease. When a patient's individual and family clinical history is characterized by multiple cases of tumors (breast and/or ovarian), which usually develop at a young age and in various family

generations, we hypothesize the existence of a mutation of the BRCA1/2 genes and we advise they undergo the Cancer Genetic Counseling process.

Due to the increasing need of Cancer Genetic Counseling and its subsequent availability, it is important to understand the psychological impact that it can have on its users. Patients being tested may experience some psychological distress during the testing process or after receiving the test results, owing to the individual and familial implications of carrying a BRCA mutation. Carriers of BRCA mutations show a higher risk of developing breast (60-70%) and ovarian (10-40%) cancer (Antoniou et al., 2003). Women with BRCA mutations then have to decide whether to pursue a specific cancer risk management strategy, such as screening, chemoprevention or prophylactic surgery (such as a mastectomy or oophorectomy), weighing up the negative consequences on procreation and body image. Furthermore, BRCA mutation carriers have to choose whether to share the newly obtained genetic information with their families: the possibility of having transmitted the genetic mutation to one's children could generate anger and guilt in an individual.

Every patient faces the genetic test and the possibility of a positive result differently. Patients may have varying degrees of awareness, based on their way of confronting stressful life events; these are called coping strategies. These strategies or efforts to tolerate certain stressful events can be more or less adaptive and can influence the psycho-physical balance of the patient, as well as the adherence to screening to reduce oncological risk.

Based on these premises, genetic testing is part of a dynamic process that encourages a comprehensive care of the patient. The most evident benefit is the chance for a better understanding of disease risk.

The multistep Cancer Genetic Counseling Model (Contegiacomo et al., 2004) tries to meet the patient's physical, mental and social needs. This in turn promotes awareness of the patient's condition in the multidisciplinary treating team (which includes an oncologist, a gynecologist, a geneticist and a psychologist). The entire process consists of three phases: pre-testing, testing and post-testing phase.

During the pre-testing phase, the subject learns about the hereditary, familial and sporadic forms of cancer and the methods available to identify the risk of developing them. The pedigree construction for at least three generations allows the geneticist to estimate the patient's risk profile. By examining the individual's clinical history, the geneticist takes into account: the age of onset of the disease, the presence of bilateral breast and ovarian tumors, multiple ovarian or breast tumors, a diagnosis of triple negative breast cancer as well as a diagnosis of male breast cancer in the family. The probability of being a carrier of a genetic mutation increases in families with a pedigree characterized by: multiple cases of breast cancer which present at a young age and in multiple generations, multiple tumors in the same individual, male breast cancer and belonging to the Ashkenazi Hebrew population. For patients who have already been diagnosed with breast or ovarian cancer, genetic testing can often help determine the prognosis and can help the treating team decide which treatments will most likely work for the patient (American Cancer Society, 2013).

Many people who undergo cancer genetic testing are anxious even before getting their test results, which may also have implications for their families. The pre-test psychological interview aims at identifying users who experience cancer genetic counseling as more stressful, assessing their coping strategies and psychological distress and at programming a possible intervention of personalized psychological support. In the case of suspected inherited risk, a genetic test is offered (testing stage) and users then have to wait at least three months for test results.

Once the molecular analysis is complete, the interdisciplinary team communicates the test results to the patient (post-test phase): here the multidisciplinary team helps the patient to read and understand the test results and also to comprehend the implications these may have on the individual and their family.

There are three possible genetic test results: positive, negative or uncertain. If the result is positive, it is identified as a pathogenetic mutation of the genes BRCA1 or BRCA2. The negative result means that no pathogenetic mutation was identified. The result is defined as "true negative" only in cases where the no mutation has been identified previously in other family members (test for the search of the "known mutation"). Lastly, the "inconclusive" or uncertain result appears in the presence of an unusual form of the BRCA gene. In a family with characteristics that are typical of hereditary cancer, this result cannot exclude the possibility of a genetic predisposition with absolute certainty.

The cause of a negative test within these families could be tied to the presence of alterations on other genes or of mutations of the gene examined, but which could not be recognized by the current laboratory procedures. The subject receives an "uncertain result" even if an unknown variant mutation is identified, for which the risk associated to developing a tumor is not known. Although cancer genetic testing is an effective instrument for cancer prevention, little is known about its psychological impact and implications. Studies in the past have shown contradictory and mixed results (Meiser, 2005). In general, the literature that has focused on psychological reactions of patients who have been subjected to genetic testing for the BRCA1 and BRCA2 genes agrees that clinically significant increases in distress are not frequent (<10%) if the patient is inserted in a Cancer Genetic Counseling program (Coyne, Benazon, Gaba, Calzone, & Weber, 2000; Smith et al., 2008; Halbert et al., 2011; Graves et al., 2012). One of the most salient limitations of the research in this field is the lack of psychological importance given to the pre-test counseling phase. However, a recent study conducted on women with and without breast cancer histories demonstrated that the result of the genetic test had no effect on the distress levels in subjects measured in the pre-test phase (Smith et al., 2008). Although in Italy the requests for Cancer Genetic Counseling are increasing, there is no Italian data that focuses on the psychological impact that the genetic testing procedure could have on its users.

2. DESIGN

This is an explorative study that focused on the psychological adaptation of patients to the Cancer Genetic Counseling process for BRCA gene testing. Subjects who requested counseling were referred by their physician or arrived spontaneously to the Cancer Genetic Counseling Unit of a hospital in Northern Italy, between 2012 and 2014. After deciding to undergo genetic testing for BRCA1 and BRCA2, subjects were informed by the doctor on how the counseling service was structured at the hospital. The process involves three different phases: in the pre-test phase the patient meets with the psychologist and then separately also with the geneticist; once the subject has been deemed suitable for genetic testing, a blood test is carried out (testing phase); lastly, the third phase involves the restitution and communication of the genetic test results.

Sixty-five women took part in the study; they were all over 18 years old and provided written informed consent before undergoing genetic counseling and testing. The women were advised to take part in Cancer Genetic Counseling by their treating oncologist or gynecologist. Using health status as an objective criterion, we distinguished between three subsamples of participants: 33 breast and/or ovarian cancer patients

(mean age = 49, SD = 11,21), 22 breast and/or ovarian cancer survivors (mean age = 50, SD = 10,41) and 10 women with strong family histories of breast and/or ovarian cancer (mean age = 41, SD = 9,93).

3. OBJECTIVES

Using these criteria as a starting point, the objective of the study was to assess the sample's psychological vulnerability experienced in the context of Cancer Genetic Counseling. Furthermore, the present study evaluated the existence of differences in distress and coping strategies between the three subsamples (breast and/or ovarian cancer patients, breast and/or ovarian cancer survivors and women with strong family histories of breast and/or ovarian cancer).

In order to identify users who experience Cancer Genetic Counseling as more stressful and to program a possible intervention of personalized psychological support, the ultimate goal of this study was to investigate the effect of coping strategies on the prediction of psychological distress among women who decide to undergo BRCA testing.

4. METHODS

4.1. Procedures

In the pre-test phase, before meeting the geneticist, subjects participated in a 45-minute psychological interview, consisting of three steps. Firstly, socio-demographic information was collected by the counselor, as well as the individual and family cancer histories, and lastly, information regarding the participant's social, religious, cultural and family resources were investigated. Thereafter, a psychologist explained the genetic counseling process and its implications; lastly, subjects completed two questionnaires, the SCL-90-R and the COPE-NVI.

The Symptom Checklist-90-R (SCL-90-R) is a self-report questionnaire that measures the presence and intensity of psychopathological symptoms and psychological distress. It is made up of 90 items that run on a 5-point Likert scale (0="Not at all"; 4= "Extremely") (Derogatis, 1994). It is used widely to measure psychological distress in clinical practice and research and has demonstrated excellent validity and reliability (Derogatis & Savitz, 2000).

The Coping Orientation to Problems Experienced- Revised Italian Version (COPE-NVI) is made up of 60 items measured on a 4-point Likert scale (1="I usually don't do this at all"; 4 = "I usually do this a lot"). This self-report questionnaire measures how people respond when they confront difficult or stressful events in their lives. It takes into consideration five coping styles: Social Support, Avoidance Strategies, Positive Attitude, Problem solving and Turning to Religion (Sica et al., 2008).

4.2. Statistical analysis

Statistical Analyses were conducted using SPSS Version 20 (IBM Corp., 2011). Descriptive statistics were generated to characterize the entire sample and the three subsamples in terms of demographics, resources, cancer history and psychological factors.

To evaluate the presence of statistically significant differences between the three subsamples regarding distress and coping strategies, the Kruskal-Wallis test and subsequently, the Mann-Whitney test for independent samples were used.

Finally, multiple regression analysis was run to study the relation between psychological variables and coping strategies.

5. RESULTS

The statistical analysis showed that 7.7% of the total sample experienced a clinically significant level of psychological distress.

Groups of participants significantly differed in relation to somatization (Figure 1), depressive symptoms (Figure 2) and hostility (Figure 3). In particular, breast and/or ovarian Cancer Survivors present a higher vulnerability to feelings and thoughts of a state of anger; significantly higher in comparison to other subsamples.

The regression analysis identified those who use the coping strategy of avoidance, predictive of an increase in symptoms of depression, anxiety and somatization, as the most vulnerable to psychological distress.

Figure 1. Somatization: mean scores between three subsamples.

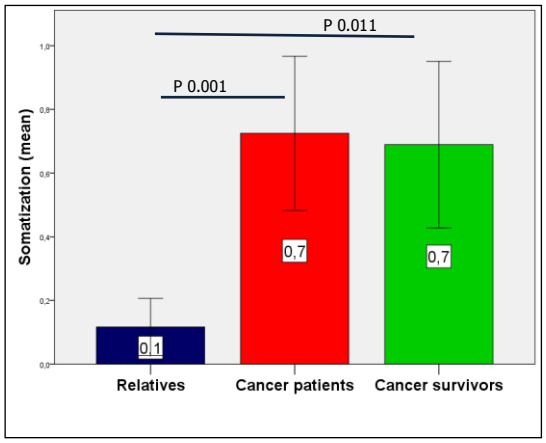


Figure 2. Depressive symptoms: mean scores three subsamples.

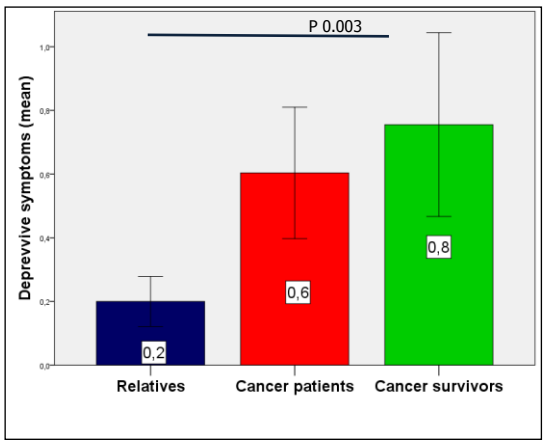
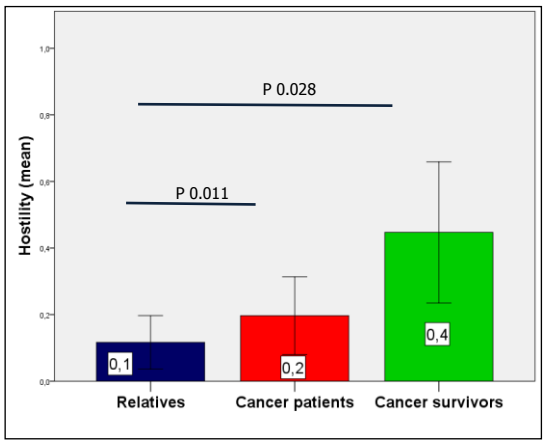


Figure 3. Hostility: mean scores between three subsamples.



6. DISCUSSION

The results of this research confirm the findings currently present in the literature. Previous research shows that abnormal psychological reactions to Cancer Genetic Counseling seem to be infrequent: in most cases, the BRCA gene test and its positive result only temporarily change the levels of psychological distress (Graves et al., 2012). Only a minority of patients (< 10%) experience a clinically significant level of psychological distress that persists over time (Coyne et al., 2000; Schwartz et al., 2002) and this was also true for our sample.

Cancer Survivors seem to have a higher risk of experiencing feelings and thoughts of a state of anger. The high level of hostility in this subsample could be explained by the fear of disease relapse. It is possible that this anger is triggered by the prospect of having a positive test result which would force the individual to face important decisions, such as a decision to undergo prophylactic surgery, which can interfere with a person's daily functioning. Therefore the risk of re-acquiring the *status* of cancer patient, because of a relapse or because of the possible preventative interventions, could make the subject feel as though they were re-living the negative experience of disease and treatment, which he or she thought they had overcome. As a consequence, it would be advisable to refer Cancer Survivors to genetic counseling at the beginning of the course of disease and treatment. Participants using avoidance coping strategies seem to be more vulnerable to psychological distress (anxiety, depression and somatization) compared to those who use problem-oriented ones, since they are hypothetically inclined to deny the mutation risk condition. Denial and mental detachment of the problem correlate with an increase of psycho-emotional distress, they also constitute a psychological vulnerability factor as they predict an increase in depressive, anxiety and somatization symptoms. Previous research has also found that the use of avoidant coping was reliably and positively associated with distress over time independent of cancer history and test results (Dougall et al., 2009). It is possible that people who use avoidance as a coping mechanism are trying to protect themselves from situations that invoke strong emotional responses; these clients may be hoping not to hear the information about their cancer risks, they may even go on to interrupt cancer risk discussions and defer genetic counseling appointments (Schneider, 2011).

Psychological intervention should therefore be focused on evaluating and strengthening levels of awareness in the patient with regards to the possibility of being a carrier of the BRCA1 or BRCA2 gene mutations, so that one does not collude with the patient and reinforce this denial through false reassurances.

7. CONCLUSIONS AND FUTURE RESEARCH

An important clinical implication of our study is that ovarian and breast Cancer Patients, Survivors and their Relatives can be actively approached and referred for Cancer Genetic Counseling without a threat to psychological functioning as only a small percentage of individuals present psychological distress during this process and these clients can be identified in the pre-testing phase and counseled through the genetic testing process.

Due to the limitation of a small sample size it was not possible to compare subsamples of female and male patients with regards to the psychological variables examined in the study. At present, to our knowledge, no study has focused on psychological adaptation of male patients during the Cancer Genetic Counseling procedure. If in the future we reach a sufficient sample size for male subjects we could create a comparison group to see if there are any significant differences between the two gender groups regarding levels of psycho-emotional distress and its respective predictors. Alternatively, we could try to compare female patients who undergo Cancer Genetic Counseling and male patients suffering from another type of cancer which has similar psychological characteristics to those measured in the female sample so that we can identify specific factors that can predict psychological distress in these two groups. The explorative study carried out focused on the psychological evaluation of the patients in the pre-test genetic phase: to strengthen the support offered it would be desirable to extend the psychological evaluation to all three phases so as to include the pre-test phase after the visit with the geneticist and the post-test phase. The exploration of psycho-emotional distress at these three phases would allow a careful monitoring of the progress of the psychological distress during the entire genetic testing process and it would allow us to see the impact that the session with the geneticist and the communication of the test results would have on the emotional functioning of an individual. Furthermore, through the use of a questionnaire that measures subjective risk, it would be possible to analyze the effect that the sessions with the psychologist and the geneticist have on the ability of estimating risk. In this way we could offer the patient a much desired, much needed, global personalized care while the subject undergoes Cancer Genetic Counseling.

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KEY TERMS AND DEFINITIONS

Cancer Genetic Counseling: a trained health care worker carries out genetic counseling. It is important to help women make informed decisions about genetic testing. In a genetic counseling session for breast and ovarian cancer, the genetic counselor will typically collect a detailed family and

medical history and then discuss questions that may arise with regards to the testing procedure. Following the genetic counseling session, a client may decide not to undergo *BRCA1/2* testing, or the client may learn that testing is not appropriate for his or her circumstances. Counseling can also help better understand the meaning of test results after genetic testing.

Cancer Genetic Testing: is a medical test to search for mutations in a patient's genes. It is a form of predictive gene testing to see if a person has a certain risk of developing cancer.

BRCA1/BRCA2: these are oncosuppressor genes that code for Breast Cancer Type 1 and 2 susceptibility proteins that are involved in repairing DNA. If these two genes are mutated then the subject is at higher risk for developing cancer.

Coping Strategy: effort or strategy that a person employs to better tolerate or master certain stressful situations.

AUTHORS INFORMATION

Full name: Valentina Di Mattei
Institutional affiliation: San Raffaele Hospital, Milan, Italy & Vita Salute San Raffaele University, Milan, Italy
Institutional address: Via Olgettina 58 & 60, Milan, Italy
Email address: dimattei.valentina@hsr.it
Short biographical sketch: obtained a Psychology degree, cum laude at the Vita-Salute San Raffaele University, Milan. She also obtained her Specialist Certification in Clinical Psychology, cum laude at the Vita-Salute San Raffaele University in Italy. She was awarded a Research Fellowship at the San Raffaele University Department of Cognitive Neurosciences. As an assistant professor of Psychodynamic psychology and Health Psychology in the Faculty of Psychology at the San Raffaele University she is author of many publications in the Health Psychology research field; this is also her clinical practice area.

Full name: Martina Bernardi
Institutional affiliation: San Raffaele Hospital, Milan, Italy
Institutional address: Via Olgettina 60, Milan, Italy
Email address: bernardi.martina@ymail.com
Short biographical sketch: obtained a Cellular and Molecular Medicine degree at the University of Bristol. She then undertook a second degree in Psychology at the University of Royal Holloway, London. After concluding her Masters degree in Clinical and Health Psychology at the Università Vita-Salute San Raffaele she is conducting her internship at the San Raffaele Hospital in Milan within the Clinical and Health Psychology Department. She has published various articles within the psycho-oncology field.

Full name: Fabio Madeddu
Institutional affiliation: Università degli Studi di Milano - Bicocca
Institutional address: Piazza dell'Ateneo Nuovo 1, Milan, Italy
Email address: fabio.madeddu@unimib.it
Short biographical sketch: Graduated from the Univeristà degli Studi di Milano reading Medicine and then specialized in Psychiatry. He is Full professor of Clinical Psychology at Univeristà Milano-Bicocca and full member I.A.A.P (International Association for Analytical Psychology). The Professor is also a Fellow of the American Academy of Psychoanalysis and Dynamic Psychiatry. His research areas are as follows: defense mechanisms, personality disorders and substance abuse.

Full name: Lucio Sarno
Institutional affiliation: San Raffaele Hospital, Milan, Italy & Vita Salute San Raffaele University, Milan, Italy
Institutional address: Via Olgettina 58 & 60, Milan, Italy
Email address: sarno.lucio@hsr.it
Short biographical sketch: Professor of Psychotherapy in the Department of Psychology at the Università Vita-Salute San Raffaele in Milan. Psychoanalytical Psychotherapist and Member of the Italian Psychoanalytical Society (SPI) where he has the role of Analyst and also of Professor. The Professor is Full Member of the International Psychoanalytic Association (IPA). He is also a Member of the Italian Institute of Group Psychoanalysis, an institute that he cofounded and was then later made President. He is author of more than 150 publications in various clinical research areas and in 2003 was made the Chief of the Clinical and Health Psychology Unit at the San Raffaele Hospital in Milan.