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The psychological impact of breast and ovarian cancer preventive options in *BRCA1* and *BRCA2* mutation carriers

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This study was performed to describe the impact of preventive options on the psychological condition of *BRCA1/BRCA2* carriers. A sample of 52 cancer-affected (C-A) and 27 cancer-unaffected (C-UN) women were enrolled after gene test disclosure (T0). Psychological evaluations were performed at T0 and 15 months later (T1). The surgical options were more likely to be chosen in C-A women (62%), although a consistent proportion of C-UN women (30%) also opt for these preventive measures. At the baseline, both samples had average anxiety and depression scores below the cut-off value, restrained average cancer worry scores and a risk perception consistent with the risk percentage provided during genetic counselling. The longitudinal results indicated no clinically meaningful variations in the anxiety and depression scores in either of the two samples. Statistically significant reductions in cancer-risk perception emerged in women who chose surgery in both C-A and C-UN women. In *BRCA1/BRCA2* mutation carriers, surveillance does not influence their initial psychological condition, whereas prophylactic surgery has a significant impact in reducing the perceived risk and worry about getting sick. C-A and C-UN women have to be considered as two separate populations of *BRCA* mutation carriers requiring personalized approaches to risk management.

Conflict of interest

The authors declare no conflict of interest.

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Hereditary susceptibility to breast cancer (BC) and ovarian cancer (OC) accounts for less than 10% of all tumour cases. The *BRCA1* and *BRCA2* germline mutations are the two main known genes associated with hereditary BC and OC. Women who carry a deleterious mutation in one of these genes have an increased risk of developing BC and OC and require an appropriate clinical management, currently based on intensive screening for the early detection of tumours and on surgical risk-reduction strategies for primary prevention.

Numerous questions remain unanswered regarding the optimal management of BC and OC risk in *BRCA*

carriers, and a careful evaluation of the positive and negative effects of the available options is needed (1, 2).

Many factors play a role in the preventive strategy choice of *BRCA* carriers; some factors depend on the information process (3, 4), whereas others rely on psychosocial variables such as risk perception, cancer worry, anxiety and depression levels, family history and having young children (3, 5–10). In particular, previous cancer-related experience seems to affect psychological status of these women (11).

The efficacy and psychological impacts of the preventive measures are still under investigation (1, 12).

Some studies report that surgery can reduce psychological morbidity but may have a negative impact on sexuality and body image (13–16). The principal reason for choosing prophylactic bilateral mastectomy (PBM) is to reduce the risk of contracting a life-threatening disease, and some studies show that no regrets regarding this choice were found (17, 18). Other studies did not show any significant differences in terms of quality of life (QOL) for both women who chose a risk-reducing strategy and those who did not (19, 20).

A number of studies have examined the psychosocial aspects correlated with the choice of the preventive strategy (5–9) as well as the impact of the choice (21–25); however, some of these studies compare women with different risk profiles irrespective of genetic test result (5, 7, 26) or focus on a specific preventive strategy, i.e. prophylactic bilateral salpingo-oophorectomy (PBSO) (27) or surveillance (28). Affected and unaffected women are often considered together (6, 8, 9); some studies (5, 11) keep them separated but aim at describing the psychological impact of genetic testing and/or counselling without considering chosen preventive strategies (29).

A multicentre, longitudinal, prospective, observational study was performed to describe the impact of preventive options on the psychological condition of two separate populations of previously cancer-affected (C-A) and -unaffected (C-UN) *BRCA1* or *BRCA2* carriers after a gene test disclosure (T0) and its modification 15 months later (T1).

The secondary aims of this study are to describe the distribution of preventive strategies, examine the baseline values and changes over time of secondary outcomes (cancer-risk perception; BC and OC worry; satisfaction regarding the chosen preventive strategy; body image and QOL) and compare T1–T0 variations in the secondary outcomes among women who chose different prevention programs (surveillance and risk-reducing surgery).

Methods

Study population

Between November 2008 and June 2010, 121 women who received a positive result of deleterious mutations in *BRCA1* and/or *BRCA2* genes at one of three Italian cancer centres (Milan, Genoa and Rome) were asked to participate in a psychological follow-up study. Failure to provide written informed consent for study participation and disease progression was the only exclusion criteria. A total of 79 *BRCA* carriers were enrolled in this study (87%) (Fig. 1).

Psychosocial assessment

Psychological distress (primary outcome variable) was evaluated by the Hospital Anxiety and Depression Scale (HADS) (30, 31). The questionnaire was translated into and validated in Italian (32).

Concerns about becoming ill with BC were evaluated by the Breast Cancer Worry Scale (33), which is composed of three items (frequency, impact on mood/disposition and impact on normal daily activities) and has been translated from English by a formal process of backward–forward translation. For this study, an adapted version for OC will also be used.

The cancer-risk perception was assessed using a five-item tool adapted from Gurmankin Levy et al. (34), whereas satisfaction with the preventive strategy chosen was evaluated with tree *ad hoc* questions adapted from previous studies (14, 35, 36). Formal forward/backward cultural adaptation was carried out for items not available in Italian language.

Body image was evaluated through an instrument adapted from the Digital Body Photo Test (37) that allows patients to indicate their own aesthetic satisfaction regarding the different parts of their body. QOL was measured by the Italian version of the MOS SF-12 questionnaire (38).

All the previous questionnaires were completed twice: a baseline evaluation 1 month after the disclosure of the genetic test result and before the preventive choice (T0), and a follow-up evaluation 15 months after baseline (T1).

Basic sociodemographic, clinical and oncological family history data were gathered at the baseline (T0), and preventive intervention choices were evaluated at 15 months from baseline (T1).

Ethical aspects

The study was approved by the Ethics Committees of all participating centres and all enrolled patients provided written informed consent.

Statistical analysis

The changes between the baseline and 15-month evaluations on each of the aforementioned primary and secondary outcomes were estimated by 95% confidence intervals (95% CIs) of the T1–T0 differences; a 95% CI not containing 0 implies a statistically significant variation between the two time points for that outcome variable.

A *t*-test for independent samples with $p = 0.05$ as significance level was applied to compare the T0–T1 differences in the primary and secondary outcome measures in women who chose surveillance to those who chose surgery.

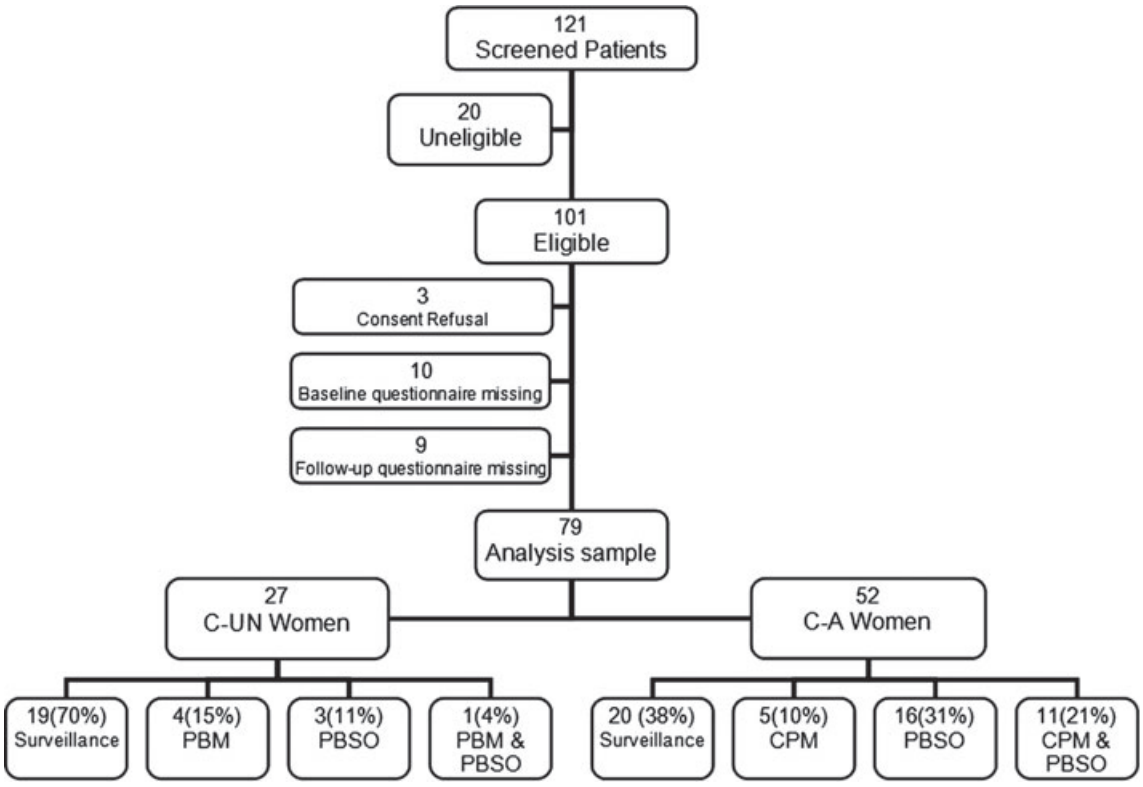

Fig. 1. Study sample.

Women undergoing PBSO and PBM were grouped together with the aim of identifying a subsample characterized by a stronger attitude to act against the risk of developing cancer ('any kind of surgery' group) compared with women opting for a watchful waiting strategy ('surveillance' group). All the tests were applied separately within the two subpopulations of C-A and C-UN women.

Results

Among the 121 patients screened, 20 were ineligible because of disease progression. Among the eligible patients, 3 refused to participate, and 10 and 9 did not complete the baseline and follow-up evaluations, respectively; a final sample of 79 women (87% of those eligible) provided complete data (Fig. 1).

The choice of preventive option, divided by previous cancer history, is shown in Fig. 1. Among the 27 C-UN women, 19 (70%) chose to follow the surveillance program, and 8 (30%) chose preventive surgery (4 chose PBM, 3 chose PBSO and 1 chose both). The choice of surveillance was less common (38%) among the 52 C-A women, with the majority choosing to undergo preventive surgery (62%) [5 chose contralateral prophylactic mastectomy (CPM), 16 chose PBSO and 11 chose both].

Table 1 reports the baseline characteristics of patients, divided by previous cancer history. C-A women had an average age of 47 years (30–70 years) and a medium education level (44% reported a senior high school diploma); the majority of these women were married or common-law wives (79%), were employed (67%) or housewives (19%) and had two children (44%). Thirty-nine women (75%) developed a single BC, eight (15%) developed multiple BC, four (8%) had an OC and one patient developed both BC and OC. Twenty-eight women (54%) had a mutation in the *BRCA1* gene, and 24 (46%) women had a mutation in the *BRCA2* gene; in 90% of cases, they were the first members of their families to be analysed. The majority of the women were menopausal, with menopause in 19% being physiological and in 25% being drug-induced (Table 1).

Tables 2 and 3 show the longitudinal outcome data (psychological aspects, risk perception, cancer worry, QOL, body image and satisfaction regarding the chosen strategy), divided by clinical condition and the cancer prevention option chosen.

C-UN women

C-UN women had average baseline anxiety and depression scores (Table 2), all the scores were below the 8-point cut-off value (31) for both women who chose surveillance and women who chose surgery. The lifetime BC- and OC-risk perception ranged from 44% to 68% in C-UN women, and the cancer-risk perception compared to that of other women was substantial at the baseline, ranging from 3.5 to 4.7 on a 1–5 scale. Consistent with anxiety scores, the Baseline Cancer Worry Scale values ranged from 5

Table 1. Demographic and clinical characteristics of the patients participating in the study

	C-UN women, $N=27$		C-A women, $N=52$	
	N	%	*N*	%
Age				
Mean (SD)	39.4 (9)		47.5 (10)	
Range	26–57		30–70	
Education				
Primary	–	–	4	8
Junior high school	6	22	13	25
Senior high school	11	41	23	44
Degree	10	37	12	23
Civil status				
Unmarried	7	26	5	9
Married/common law	17	63	41	79
Divorced/separated	2	7	4	8
Widowed	1	4	2	4
Occupation				
Employed	23	85	35	67
Housewife	4	15	10	19
Pensioner	–	–	6	12
Unemployed	–	–	1	2
Number of children				
0	10	37	7	13
1	5	19	18	35
2	10	37	23	44
3	2	7	4	8
Previous BC/OC				
Breast (single)	–	–	39	75
Breast (multiple)	–	–	8	15
Ovary	–	–	4	8
Breast (single) and ovary	–	–	1	2
Mutation				
BRCA1	20	74	28	54
BRCA2	7	26	24	46
Mutation already in family				
No	4	15	47	90
Yes	23	85	5	10
Menopausal status				
No	24	89	16	31
Drug induced (definitive)	–	–	13	25
Drug induced (temporary)	–	–	8	15
Caused by surgery	–	–	5	10
Physiological	3	11	10	19
Preventive strategies				
Surveillance	19	70	20	38
PBM	4	15	5	10
PBSO	3	11	16	31
PBM and PBSO	1	4	11	21

BC, breast cancer; C-A, cancer-affected; C-UN, cancer-unaffected; OC, ovarian cancer; PBM, prophylactic bilateral mastectomy; PBSO, prophylactic bilateral salpingo-oophorectomy.

to 7.5, which indicated a moderate level of concern regarding cancer. The QOL SF-12 global indexes for this group were approximately 54 (physical QOL) and 47 (psychological QOL). Baseline body image data indicated a medium level of satisfaction in both groups of patients.

When the T1–T0 time variations were examined in women who chose surveillance (Table 2, column 5), no statistically significant differences were found in any of the outcome measures considered, whereas in women who chose surgery (Table 2, column 8), considerable and statistically significant reductions in both the perception of risk of developing BC and in the BC worry scores were reported. The remaining outcomes did not show any relevant changes. In both groups of women (surveillance or surgery), the reported satisfaction with the chosen strategy is positive. The results of the comparison between T1 and T0 variations in 'surveillance' group and 'any kind of surgery' group are reported in the last column of Table 2. Statistically significant differences between the two groups were reported for cancer-risk perception and worry outcomes, with larger modifications in women undergoing surgery (32.5 *vs* 2.28 reduction for lifetime BC-risk perception, $p=0.01$ and 2.75 *vs* 0.1 reduction for cancer worry, $p=0.002$).

A cancer-risk perception greater than 20% after surgery indicates that women overestimated their risk perception in 62% of cases for BC and in 50% of cases for OC (data not shown). The physical and psychological QOL SF-12 scores did not show statistically significant differences.

C-A women

At baseline, the average depression scores were below the 8-point cut-off value for all C-A women (Table 3), and the average anxiety scores were above the 8-point cut-off value for those who chose surgery (56% $\geq$ 8).

The lifetime BC and OC risk perception values were 49% and 30%, respectively, and the cancer-risk perception compared to that of other women of a similar age ranged from 3 to 4 (on a 1–5 scale). The Baseline Cancer Worry Scale values ranged from 5.6 to 6.9 (on a 3–15 scale), which indicated a moderate level of concern regarding cancer. The physical QOL SF-12 scores (49.08 and 45.03, respectively, for surveillance and surgery groups) were slightly lower than the average score of 51 in healthy Italian women aged 45–54 years, whereas the average psychological QOL score for the 'surveillance' group (48.8), but not for 'any kind of surgery' group (44.4), was in accordance with the average score of 48.5 in the national sample (39). The body image data indicated a medium–low baseline level of satisfaction in both groups of patients.

In 'surveillance' group (Table 3, column 5), no relevant T1–T0 variations were found, whereas in 'any kind of surgery' group (Table 3, column 8), statistically significant differences were found for BC and OC risk perception (−15.6 and −16.7, respectively) and for perceived risk with respect to women of a similar age (−0.82 and −1.26, respectively, for BC and OC). Consistently, the level of concern regarding the development of cancer decreased for both the breast (−0.54, not statistically significant) and the ovary (−0.85, CI: −1.67/−0.03) in women who chose surgery.

Table 2. Longitudinal outcome data by cancer prevention choice in C-UN women

		'Surveillance' group ($n = 19$)			'Any kind of surgery' group ($n = 8$)			
	Range	T0	T1	T1–T0 difference[a] (95% CI)	T0	T1	T1–T0 difference[a] (95% CI)	p[b]
Hospital Anxiety and Depression Scale (HADS)								
Anxiety	0–21	7.26	7.21	−0.05 (−1.09/0.98)	6.5	6.38	−0.12 (−2.04/1.79)	NS
Depression	0–21	5	5.37	0.37 (−0.91/1.65)	4.5	4.5	0.00 (−2.75/2.75)	NS
Cancer-risk perception								
Probability to develop breast cancer (BO) during lifetime (%)	0–100%	60.06	57.78	−2.28 (−12.59/8.03)	68.75	36.25	−32.50 (−60.94/−4.06)	0.01
Risk of developing BO compared to other women of the same age	1–5	3.89	3.95	0.05 (−0.20/0.31)	4.75	3.25	−1.50 (−2.84/−0.16)	0.07
Probability to develop ovarian cancer (OC) during lifetime (%)	0–100%	44.17	47.78	3.61 (−12.29/19.52)	58.75	27.13	−31.63 (−65.20/1.95)	0.02
Risk of developing OC compared to other women of the same age	1–5	3.53	3.63	0.11 (−0.35/0.56)	4.5	3	−1.50 (−3.11/0.11)	0.01
Cancer Worry Scale								
Breast	3–15	5.58	5.47	−0.11 (−0.70/0.49)	7.5	4.75	−2.75 (−5.15/−0.35)	0.002
Ovary	3–15	4.95	4.79	−0.16 (−0.83/0.51)	6.5	4.13	−2.38 (−5.20/0.45)	0.2
Quality of life (SF-12)								
Physical	0–100	54.34	53.66	−0.68 (−1.96/0.60)	55.22	52.43	−2.80 (−6.42/0.82)	NS
Psychological	0–100	46.97	47.17	0.20 (−4.41/4.81)	47.41	49.42	2.01 (−7.83/11.85)	NS
Body image								
Overall aesthetic satisfaction	0–10	6.95	6.99	0.04 (−0.28/0.37)	6.77	6.48	−0.29 (−1.24/0.66)	NS
Breast aesthetic satisfaction	0–10	6.91	6.88	−0.03 (−1.04/0.97)	6.36	6.14	−0.21 (−2.28/1.85)	NS
Choice satisfaction (15 months after test)	1–5		3.84			4.38		NS

[a]Positive differences indicate an increase in outcome and negative differences indicate a decrease in outcome.
[b]Independent samples. Student's *t*-test comparing the T1–T0 variations in women who chose surveillance *vs* women who chose surgery.

Table 3. Longitudinal outcome data by cancer prevention choice in C-A women

		'Surveillance' group ($N = 20$)			'Any kind of surgery' group ($N = 32$)			
	Range	T0	T1	T1–T0 difference[a] (95% CI)	T0	T1	T1–T0 difference[a] (95% CI)	p[b]
Hospital Anxiety and Depression Scale (HADS)								
Anxiety	0–21	7.58	6.85	−0.72 (−2.26/0.81)	8.46	8.59	0.13 (−0.91/1.16)	NS
Depression	0–21	4.95	5.55	0.60 (−0.40/1.60)	5.41	6.34	0.94 (−0.16/2.04)	NS
Cancer-risk perception								
Probability to develop breast cancer (BO) in lifetime (%)	0–100%	49.21	55.26	6.05 (−8.99/21.09)	48.60	33.00	−15.60 (−29.02/−2.18)	0.03
Risk of developing BO with respect to other women of the same age	1–5	3.95	3.60	−0.35 (−0.70/0.00)	4.00	3.18	−0.82 (−1.41/−0.23)	NS
Probability to develop ovarian cancer (OC) during lifetime (%)	0–100%	26.42	31.42	5.00 (−15.07/20.69)	36.67	19.93	−16.74 (−26.10/−7.38)	0.02
Risk of developing OC with respect to other women of the same age	1–5	3.31	3.13	−0.19 (−0.90/0.47)	3.79	2.53	−1.26 (−1.98/−0.55)	0.02
Cancer Worry Scale								
Breast	3–15	6.90	6.95	0.05 (−1.20/1.30)	6.79	6.25	−0.54 (−1.43/0.36)	NS
Ovary	3–15	5.56	6.00	0.44 (−1.67/2.39)	5.95	5.10	−0.85 (−1.67/−0.03)	NS
Quality of life (SF-12)								
Physical	0–100	49.08	45.51	−3.56 (−8.18/1.05)	45.03	46.92	1.89 (−1.34/5.12)	0.04
Psychological	0–100	48.86	51.21	2.35 (−2.75/7.45)	44.45	46.44	1.99 (−1.90/5.88)	NS
Body image								
Overall aesthetic satisfaction	0–10	6.50	6.25	−0.25 (−0.88/0.38)	6.23	6.25	0.02 (−0.43/0.47)	NS
Breast aesthetic satisfaction	0–10	5.94	5.38	−0.56 (−1.34/0.22)	4.56	4.39	−0.17 (−1.02/0.69)	NS
Choice satisfaction (15 months after test)	1–5		3.65			3.85		NS

[a]Positive differences indicate an increase in outcome and negative differences indicate a decrease in outcome.
[b]Independent samples. Student's *t*-test comparing the T1–T0 variations in women who chose surveillance *vs* women who chose surgery.

A cancer-risk perception greater than 20% after surgery indicates that women overestimated their risk perception in 46% of cases for BC and in 34% of cases for OC (data not shown). Both groups of patients reported similar medium/high levels of satisfaction with their choices.

Statistically significant differences in the T1–T0 analyses between the 'surveillance' and 'any kind of surgery' groups were reported for the lifetime cancer-risk perception (Table 3, last column), with a greater reduction observed for women undergoing surgery (15.6 reduction *vs* 6.05 increase for BC risk, $p = 0.03$, and 16.7 reduction *vs* 5.0 increase for OC risk, $p = 0.02$). A smaller, but still statistically significant, group difference was also reported for the perceived risk of developing OC with respect to other women of a similar age (1.26 *vs* 0.19 reduction, $p = 0.02$). The physical dimension of QOL showed a slight improvement in women who chose surgery, it decreased in women who chose surveillance (1.89 increase *vs* 3.56 decrease, $p = 0.04$).

Discussion

In agreement with previous results (40, 41), the present data indicated that surgical options are more common in C-A women (62%); however, a consistent proportion of C-UN women (30%) also chose this type of intervention, especially prior to the age of 44 (75%).

In accordance with another Italian study performed on a similar population (42), the average baseline anxiety and depression scores were below the 8-point cut-off value in both C-A and C-UN women, with the exception of anxiety scores in C-A women who chose surgery (56% scored above the cut-off). Baseline anxiety and depression scores in our sample are comparable to those of Italian BC women (anxiety 7.5; depression 4.0) (32) and to international norm scores [anxiety mean values range from 3.6 (Hong Kong) (43) to 6.4 (UK) (44) and depression means are between 3.3 (Hong Kong) (43) and 6.6 (Korea) (45)] except for C-A women who seem to be more anxious (anxiety 7.6 'surveillance group' and 8.5 'surgery group').

Cancer worry was also restrained at the baseline (scores ranged from 5 to 7.5 on a 3–15 scale). The perceived risk was consistent with the level of risk described during genetic counselling for BC, but OC-risk perception is overestimated by both C-UN and C-A women; this is probably because of the difficulties in obtaining an early diagnosis and to the poor prognosis, as communicated during genetic counselling.

The longitudinal results indicated no clinically meaningful variations in anxiety and depression scores, with the upper limits of the confidence intervals for the T1–T0 differences being lower than 3 points on a 0–21 scale for all subgroups of patients.

With regard to the secondary outcomes, women who chose surveillance (both C-A and C-UN) did not show any statistically significant modifications in any of the outcomes examined. In contrast, and in agreement with previous studies (27), statistically significant reductions in cancer-risk perception emerged in women who chose surgery, and the differences between preventive choice options are statistically significant in both C-A and C-UN women. The data suggest that these women understood the effectiveness of the surgery (46, 47) in reducing cancer risk.

Unexpectedly, the risk perception after surgery (at T1) still remained greater than the actual residual risk after the intervention for both subgroups. Most women felt that their BC risk was not eliminated following prophylactic surgery: 62% of C-UN and 46% of C-A women reported a risk perception greater than 20%. A conspicuous number of women overestimated their OC-risk perception after surgery: 50% of C-UN and 34% of C-A women reported a risk perception greater than 20%.

These data are consistent with previous results (27, 48) showing that women overestimated their risk even after prophylactic surgery. Time-based modifications of cancer worry scores show a similar pattern, with statistically significant differences when comparing the choice of preventive strategy found only in C-UN women.

C-A women did not report statistically significant cancer worry reductions at T1, even if they reported a significant risk perception reduction after surgery. It could be hypothesized that cancer worry in C-A women does not depend only on genetic-risk perception. It must be considered a possibility that the psychological experiences of affected women are also influenced by the risk of recurrence of the past disease and this could also explain their anxiety level that is slightly over the norm scores.

A previous history with cancer seems to be a more sensitive factor than the general distress indexes (i.e. anxiety and depression) that were applied in previous studies (9).

In agreement with previous studies (48), the QOL in C-UN women was comparable with the general population and with healthy Italian women aged 35–44 years (Physical Component Summary = 53, Mental Component Summary = 50) (39). However, the physical QOL in C-A women was slightly lower at baseline (when compared with healthy Italian women aged 45–54 years), and at T1, it slightly improved in women who chose surgery but decreased in women who chose surveillance.

The levels of satisfaction with the preventive choice are rather high in the four subgroups of patients, in particular for C-UN women who chose surgery (4, 3, on a scale of 1–5), with no statistically significant differences found when comparing between chosen preventive strategies. These results confirm previous reports (49).

Our data suggest that C-A and C-UN women have different profiles with regard to demographical and clinical characteristics, preventive choice, risk perception, cancer worry, QOL and satisfaction scores. These factors could influence both the choice and the impact of preventive strategies. For this reason, C-A and C-UN

women would require a personalized approach to cancer risk management centred on maintaining a balance between the preventive choices, the psychological condition and their life project, which is for most of them yet to be defined (childbearing and employment career).

In conclusion, a deeper knowledge of the impact of preventive strategies on the psychological condition allows to better manage decision-making processes of BRCA1/2 carriers. In particular, our results not only highlight the positive impact of risk-reducing surgery in reducing the perceived risk and cancer worry but also the importance of choosing a strategy consistent with one's risk profile and emotional condition. The different profile showed by C-A and C-UN suggests the need for a personalized approach for C-UN women tailored on their specific needs.

Limitations

The sample sizes of the groups compared are limited particularly in the 'any kind of surgery' group of C-UN women. Considering our enrolment period and given that we excluded high-risk women without BRCA1-2 mutation, our sample size is comparable with other studies (9, 27, 50). Although a low sample size implies low study power, the results on the main outcome measures (anxiety and depression) clearly indicate trivial T1−T0 variations in each of the patient subgroups examined, with the 95% CIs for T1−T0 differences all being narrower than −3/+3 on a 0−21 scale. However, T1−T0 changes did reach statistical significance when examining cancer-risk perception and BC/OC worry.

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