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BRCA mutation carriers' perceptions on postmenopausal hormone therapy: An Italian study

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Abstract

Objective: To evaluate the actual perceptions of postmenopausal hormone therapy (HT) in BRCA mutation carriers (BRCAmc) in comparison with women from the general population.

Methods: Questionnaire-based study of 83 BRCAmc and a control group of 89 women without a genetic mutation. Perceptions were evaluated by specific questions and Likert scales (−5–+5).

Results: Present and past users of HT were more frequent in the control group ($p = 0.01$), with a longer time of use ($p = 0.03$). The preferred route of administration of HT was 'oral' (54.6%). The most frequently reported adverse effect of HT was venous thrombosis (0.8), while a protective effect on bone health was reported. No noticeable beneficial effects of HT have been recognised for hot flushes (0.2) and vaginal dryness (0.1). The most frequently perceived beneficial and adverse effects of HT were not significantly different between BRCA mutation carriers and controls. The greatest oncological fear was breast cancer (1.0). The protective role of HT on colorectal cancer was not known (0.1). These oncological impacts were mostly overestimated in BRCAmc, however this was not significant. Few BRCAmc would think of taking HT after risk-reducing surgeries.

Conclusions: Knowledge of the effects of HT on BRCAmc is relatively poor and they are likely to overstate its negative effects and underestimate its health benefits; however, this is not significant in comparison to the general population. More and better information should be given to BRCAmc to allow them to make informed decisions about the use of HT, especially before undergoing risk-reducing surgeries.

KEYWORDS
BRCA, breast cancer, cancer, oncology, postmenopausal hormone therapy, risk-reducing surgery, RRSO, RRM, side effects

1 | INTRODUCTION

Postmenopausal hormone therapy (HT) is used to relieve menopausal symptoms. It is the principal therapy for urogenital and vasomotor symptoms of menopause.[1] HT offers multiple additional beneficial effects on women's health: it has been approved by the Food and Drug Administration (FDA) for the prevention and management of osteoporosis.[2] It also shows beneficial results on cognitive function and, possibly, the prevention of dementia.[2,3] Furthermore, as confirmed by the Women's Health Initiative (WHI) study, it can exert a protective effect on the cardiovascular system if started at the beginning of the menopause,[1,2] and can also improve sleep and mood disorders.[2–5]

Recent studies have demonstrated that this therapy can also be safely used in women with a familial risk of breast and/or ovarian cancer, such as BRCA1 and 2 mutation carriers. Short-term HT use has not been associated with an increased breast cancer risk, in particular in women who have undergone previous risk reducing mastectomy (RRM).[6] Before the age of 51 and after risk-reducing salpingo-oophorectomy (RRSO) and/or premature ovarian insufficiency (POF), the benefits of HT overcome its risks, if there are no contraindications.[7] After the age of 51, it is important to only treat women with debilitating vasomotor symptoms, after alternative therapies have failed.[7–12] For these high-risk patients, the decision to use HT is more complex and should be discussed in detail before RRSO surgery. Some BRCA mutation carriers undergoing RRSO are not candidates for HT due to a personal history of breast cancer. For the remainder, the risks of HT must be balanced with the impact of early menopause on long-term health and quality of life.[11]

There are different formulations for postmenopausal HT: oestrogen only (indicated for women who have previously undergone a hysterectomy), oestrogen combined with progestin (indicated for women who did not have their uterus removed) and also 'progestin-free' drugs, such oral tibolone and combinations of oestrogen with bazedoxifene (tissue selective oestrogen complex).[7] HT can be taken at different doses and in different ways: orally, as a patch, or as a transdermal or vaginal cream.[2]

Several studies in various countries have shown that women have little knowledge of the menopause and the benefits and risks of HT.[13–21] However, there are currently no published studies evaluating the awareness of the effects of HT in women at high-risk of developing breast and/or ovarian cancer, such as BRCA mutation carriers.

The objective of this study is, therefore, to evaluate the current knowledge of the benefits and risks of HT in women at high-risk of developing breast and/or ovarian cancer carrying a BRCA mutation, also assessing the main concerns about taking such therapy, in comparison with the responses of women from the general population.

2 | METHODS

2.1 | Study design

This is a cross-sectional, observational study performed from December 2019 to May 2020 at Modena family cancer clinic (MFCC), one of four hub centres of our region (Emilia-Romagna), which identifies families with increased hereditary cancer risk. Postmenopausal women with a pathogenic germline BRCA mutation were recruited (both naturally and surgically-occurred menopause). A control group of women without a genetic mutation was obtained from a group of postmenopausal subjects with no previous oncological diseases evaluated for a routine visit at the general gynaecological service of the same hospital in April and May 2020 ('Ambulatorio Divisionale'). This service is where general practitioners send patients for routine gynaecological examinations. Therefore, they are healthy women who did not present particular gynaecological disorders or complaints. The menopausal status was classified as amenorrhoea longer than 12 months.

2.2 | Evaluated variables

During the routine gynaecological examination, clinical data of included women were collected: age, parity, number of vaginal or caesarean births, abortions, and gynaecological (hysterectomy salpingo-oophorectomy [RRSO]) and breast (mastectomy, quadrantectomy, risk-reducing mastectomy [RRM]) surgeries previously performed. After a detailed counselling session about the study, the woman who chose to participate signed an informed consent. Once included in the study, women were given a different questionnaire depending on the group they belonged to (with and without genetic mutation; Table S1).

For both groups of women (with and without mutation), questionnaires collected data on the type of HT used (oral, transdermal, vaginal cream), the brand name of the product used, and the use (current, past, and never used) and duration of use (months/years). Women were asked to evaluate, in their opinion, how much HT could affect the risk of developing some types of cancer (breast, ovary, colon, uterine body and uterine cervix), or diseases (venous thrombosis, breast cysts, osteoporosis, bone fractures, cardiovascular diseases, early dementia and depression), or classical menopausal symptoms (headache, weight gain, reduced sexual desire, vaginal dryness, dyspareunia, increased appetite, mood swings, hot flashes, sleep disturbances and urinary incontinence) using a Likert scale from −5 to +5. For cancers and diseases, the following values were used: −5 = reduces the risk of onset, 0 = has a neutral effect, +5 = increases the risk of onset, while for symptoms the following values were applied: −5 = worsens with HRT, 0 = neutral effect, and +5 = improves with HT (Table S1).

Participants' preferences regarding the different routes of administration of HT, their opinion concerning the quality of the information they were provided with by health care providers (HCP), their use of a hormonal contraceptive method in the past (present or past users) and, if so, which one and for how long (months/years) were also evaluated.

Only in the group of women with a genetic mutation, whether they would take the therapy after a RRSO and/or RRM and how safe they would feel taking HT was asked using a visuo-analogue scale (VAS) from 0 to 10 (0 = very insecure, 10 = very safe). Specific questionnaires used in this study for women with and without mutation are reported in Table S1 in the English translation. We used the same questionnaires applied in a recent Italian study[22] and validated the simple questions in a previous pilot evaluation.

2.3 | Ethics and statistics

The results of this study are part of a larger project named 'Quality of (reproductive) life in women at increased risk of hereditary and/or ovarian cancer' approved by the Area Vasta Emilia Nord Ethics Committee (Reference No. 515, 2019). The primary endpoint of this larger trial will be to study the type and intensity of climacteric symptoms, the reduced quality of life, sexual and mental health, and alterations in bone mineral density and biomarkers of cardiovascular disease, in BRCA mutation carriers according to RRSO status and timing. A specific informed consent was obtained from each woman for the use of her personal data in the research analysis.

The answers of women with and without mutation were analysed and compared. The prevalence in the different groups was calculated. When necessary, the prevalence was compared by means of contingency tables. Comparisons between groups for continuous variables were performed by Student's test. Results of the VAS from 0 to 10 (0 = very insecure, 10 = very safe) were categorised as 0–3: low, 4–7: medium, and 8–10: high. The statistical analysis was performed using the statistical package StatView (v 5.01.98; SAS Institute Inc., Cary, NC). Correlations were considered significant at a p-value <0.05. The results of the continuous data are expressed as the mean ± standard deviation (SD).

2.4 | Sample size calculation

Assuming a pooled SD of 1 unit, the study would require a sample size of 63 women for each group (i.e., a total sample size of 126, assuming equal group sizes), to achieve a power of 80% and a level of significance of 5% (two sided), for detecting a true difference in means of 0.5 unit in some Likert Scale values between different groups.

3 | RESULTS

3.1 | Study group

A population of 172 women (mean age: 54.4 ± 7.0 years, range 37.9–74.0 years) was included in the study and completed the specific questionnaires. Of these women, 89 (51.7%) did not have any known genetic mutation (control group), while 83 (48.3%) were BRCA mutation confirmed carriers (BRCA1: 42 [50.6%], BRCA2: 41 [49.4%]) of a similar age. The features of the included women are shown in Table 1. There were only 19/172 (11.0%) present users of HT in the whole group are at the time of study inclusion: present and past users of HT were more frequent in the control group ($p = 0.01$), with a longer time of use ($p = 0.03$). The rate of women who had already undergone RRSO in mutation carriers was 42/83 (50.6%), while those with previous RRM was 11/83 (13.3%).

The preferred route of administration of an eventual HT was oral in 94/172 (54.6%) women, transdermal by a patch in 56/172 (30.2%) women and vaginal by a cream in 20/172 (11.6%) women; the choice was not different between BRCA mutation carriers and the control group: oral (60% vs. 49%), transdermal (29% vs. 36%) and vaginal (8% vs. 15%; $p = 0.23$).

3.2 | Knowledge of effects of hormone therapy on diseases development and on menopausal symptoms

The answers to the questions 'How much can HT increase or reduce the risk of developing these diseases?' and 'How much can HT improve or worsen these symptoms?' are reported in Table 2 for the whole study group and for BRCA mutation carriers versus the control group separately.

The most commonly reported adverse effect associated with HT was venous thrombosis (0.8 ± 0.2), followed by the development of breast cysts (0.7 ± 0.2). A protective role of HT was reported for bone fracture (–0.9 ± 0.2), osteoporosis (–0.7 ± 0.2), depression (–0.6 ± 0.2) and dementia (–0.4 ± 0.2). However, these effects were generally underestimated (<1 out of 5 of possible Likert Scale), especially in BRCA mutation carriers, although these results were not statistically significant ($p > 0.05$; Table 2). Interestingly, the most significant side effects of HT were weight increase (0.7 ± 0.2), headache (0.5 ± 0.2) and increased appetite (0.3 ± 0.2). The impact of these was generally overestimated in mutation carriers. No particular beneficial effect of HT was recognised for hot flushes (0.2 ± 0.3), mood swings (0.1 ± 0.2), sleep disorders (0.1 ± 0.2) and vaginal dryness (0.1 ± 0.2), if not substantially neutral. This was confirmed for both BRCA mutation carriers and the control group. These answers were not statistically different in the BRCA mutation carrier females with and without previous RRSO or RRM ($p > 0.05$).

TABLE 1 Features of $n = 172$ women included in the study with or without BRCA gene mutation

	BRCA mutation carriers ($n = 83$)	Control group ($n = 89$)	p
Mutation type	BRCA1: 42 (50.6%)	/	-
	BRCA2: 41 (49.4%)	/	-
Age (years old)	55.0 ± 8.2	53.9 ± 5.9	0.3
Nulliparous (*n*, %)	11 (13.3%)	14 (15.7%)	0.65
HT use (*n*, %)			
Present users	6 (7.2%)	13 (14.6%)	0.01
Past users	6 (7.2%)	17 (18.9%)	-
Never	71 (85.6%)	59/89 (66.3%)	-
Duration of use (months)	17.1 ± 17.2	41.7 ± 50.2	0.03
Past hormonal contraceptives users	52 (62.7%)	65 (73%)	0.12

Abbreviation: HT; postmenopausal hormone therapy.

TABLE 2 Mean ± Standard error (Likert scale from −5 to +5) sort in descending order to the questions 'How much can HT increase or reduce the risk of developing these diseases?' and 'How much can HT improve or worsen these symptoms?' for the whole study group in comparison with what emerges from the literature (in the general population) and for BRCA mutation carriers versus control group separately

	How much does HT increase or reduce the risk of developing these diseases?				
	Total group ($n = 172$)	Evidence from the literature	BRCA mutation carriers ($n = 83$)	Control group ($n = 89$)	p
Venous thrombosis	0.8 ± 0.2	Increased risk	0.9 ± 0.2	0.6 ± 0.3	0.52
Breast cysts	0.7 ± 0.2	Increased risk	1.0 ± 0.2	0.5 ± 0.3	0.32
Cardiovascular diseases	0.1 ± 0.2	Reduced risk	0.4 ± 0.3	−0.2 ± 0.2	0.16
Dementia	−0.4 ± 0.2	Uncertain	−0.2 ± 0.2	−0.5 ± 2.6	0.39
Depression	−0.6 ± 0.2	Uncertain	−0.4 ± 0.3	−0.7 ± 0.2	0.16
Osteoporosis	−0.7 ± 0.2	Reduced risk	−0.4 ± 0.3	−1.0 ± 0.3	0.14
Bone fractures	−0.9 ± 0.2	Reduced risk	−0.5 ± 0.3	−1.2 ± 0.3	0.09
	How much does HT improve or worsen these symptoms?				
Weight increase	0.7 ± 0.2	Uncertain	1.2 ± 0.3	0.3 ± 0.4	0.07
Headache	0.5 ± 0.2	Uncertain	1.0 ± 0.2	0.2 ± 0.3	0.05
Increased appetite	0.3 ± 0.2	Uncertain	0.6 ± 0.2	0.0 ± 0.3	0.14
Hot flashes	0.2 ± 0.3	Reduced risk	0.4 ± 0.3	0.1 ± 0.4	0.57
Mood swings	0.1 ± 0.2	Reduced risk	0.4 ± 0.3	−0.1 ± 0.3	0.2
Sleep disorders	0.1 ± 0.2	Uncertain	0.3 ± 0.3	0.0 ± 0.3	0.42
Vaginal dryness	0.1 ± 0.2	Reduced risk	0.2 ± 0.3	0.0 ± 0.4	0.68
Dyspareunia	0.0 ± 0.2	Reduced risk	−0.1 ± 0.2	0.0 ± 0.3	0.87
Reduction of libido	−0.1 ± 0.2	Reduced risk	0.1 ± 0.3	−0.3 ± 0.3	0.41
Urinary incontinence	−0.2 ± 0.2	Reduced risk	0.2 ± 0.2	−0.5 ± 0.3	0.09

Abbreviation: HT; postmenopausal hormone therapy.

TABLE 3 Mean ± Standard error (Likert scale from −5 to +5) sort in descending order to the question 'How much can HT increase or reduce the risk of developing these cancers?' for the whole study group in comparison with what emerges from the literature (in the general population) and for BRCA mutation carriers versus control group separately

	How much does HT increase or reduce the risk of developing these cancers?				
	Total group (n = 143)	Evidence from the literature	BRCA mutation carriers (n = 54)	Control group (n = 89)	p
Breast cancer	1.0 ± 0.3	Increased risk	1.1 ± 0.3	0.9 ± 0.4	0.63
Ovarian cancer	0.5 ± 0.2	Increased risk	0.7 ± 0.3	0.4 ± 0.3	0.53
Uterine body cancer	0.4 ± 0.2	Neutral effect	0.6 ± 0.3	0.4 ± 0.3	0.60
Uterine cervix cancer	0.4 ± 0.2	Neutral effect	0.8 ± 0.3	0.3 ± 0.3	0.33
Colorectal cancer	0.1 ± 0.2	Reduced risk	0.3 ± 0.3	−0.1 ± 0.3	0.31

Abbreviation: HT; postmenopausal hormone therapy.

3.3 | Knowledge of effects of hormone therapy on cancer development

For the analysis of this specific topic, we decided to exclude the considerable group of breast and ovarian cancer survivors in the BRCA mutation carriers group (n = 29 [34.9%], past breast cancer n = 25, past ovarian cancer n = 3 and past ovarian and breast cancer n = 1).

The answers to the question 'How much can HT increase or reduce the risk of developing these cancers?' are shown in Table 3.

The greatest concern was about breast cancer (1.0 ± 0.3) followed by ovarian cancer (0.5 ± 0.2), uterine body cancer (0.4 ± 0.2) and uterine cervix cancer (0.4 ± 0.2). The protective role of HT against colorectal cancer was not known (0.1 ± 0.2). These effects were generally overestimated in BRCA mutation carriers, although the results were not statistically significant ($p > 0.05$; Table 3).

3.4 | Counselling quality of health care providers and willingness to initiate hormone therapy after risk-reducing salpingo-oophorectomy/ risk-reducing salpingo-oophorectomy

Overall, most women (102/172, 59.3%) stated that they received adequate information about HT, with similar results in BRCA mutation carriers versus the control group. The percentage of women who considered the information received to be inadequate was significantly lower in women who had never used HT in comparison to those who used HT (50.8% vs. 85.7%; $p < 0.0001$). Our analysis shows that the majority of BRCA mutation carriers (67.5%) are worried that the use of HT may increase their risk of developing cancer (Figure 1).

Indeed, in mutation carriers the willingness to take HT was generally very low and no significantly different emerged after undergoing any of the two risk-reducing surgeries, RRSO or RRM (mean 3.4 ± 0.4 vs. 3.5 ± 0.4 VAS, $p = 0.81$, rate in Figure 2).

4 | DISCUSSION

4.1 | Main results

The results of the present study demonstrate that, in women at high risk of developing breast and ovarian cancer, the knowledge of menopausal symptoms and possible HT beneficial effects is relatively low. BRCA mutation carriers are likely to overstate the negative effects of HT and underestimate its health benefits. It should be pointed out, however, that we did not find substantial differences in their perceptions in comparison to the general population.

Therefore, it is essential to raise awareness regarding menopausal symptoms and management options, not only in the general population, but also in the high-risk group. The rate of use of postmenopausal HT is very low in our sample (11.0%), and was mainly reported in women without a BRCA mutation.

The most frequently reported HT-related adverse effect was venous thrombosis. On the other hand, with a similar potency, a protective effect on bone, depression and dementia was reported. Interestingly, less is known about the classical favourable effects on hot flushes, mood swings, sleep disorders and vaginal dryness achieved with HT use, also in women from the general population.

The greatest fear on the oncological side was, as expected, breast cancer, especially in this high-risk population. Concomitantly, the protective role of HT use on colorectal cancer was not properly understood. BRCA mutation carriers tended to report an overestimation of the carcinogenetic risks associated with HT, although this was not significant.

Overall, detailed information tends to increase the willingness to use HT: nevertheless, few BRCA mutation carriers would think of taking HT after risk-reducing surgeries, similarly after RRSO or RRM.

4.2 | Clinical implications

HT use has declined by up to 62% since the publication of WHI study.[23,24] Our data indicate that education about the effects of HT

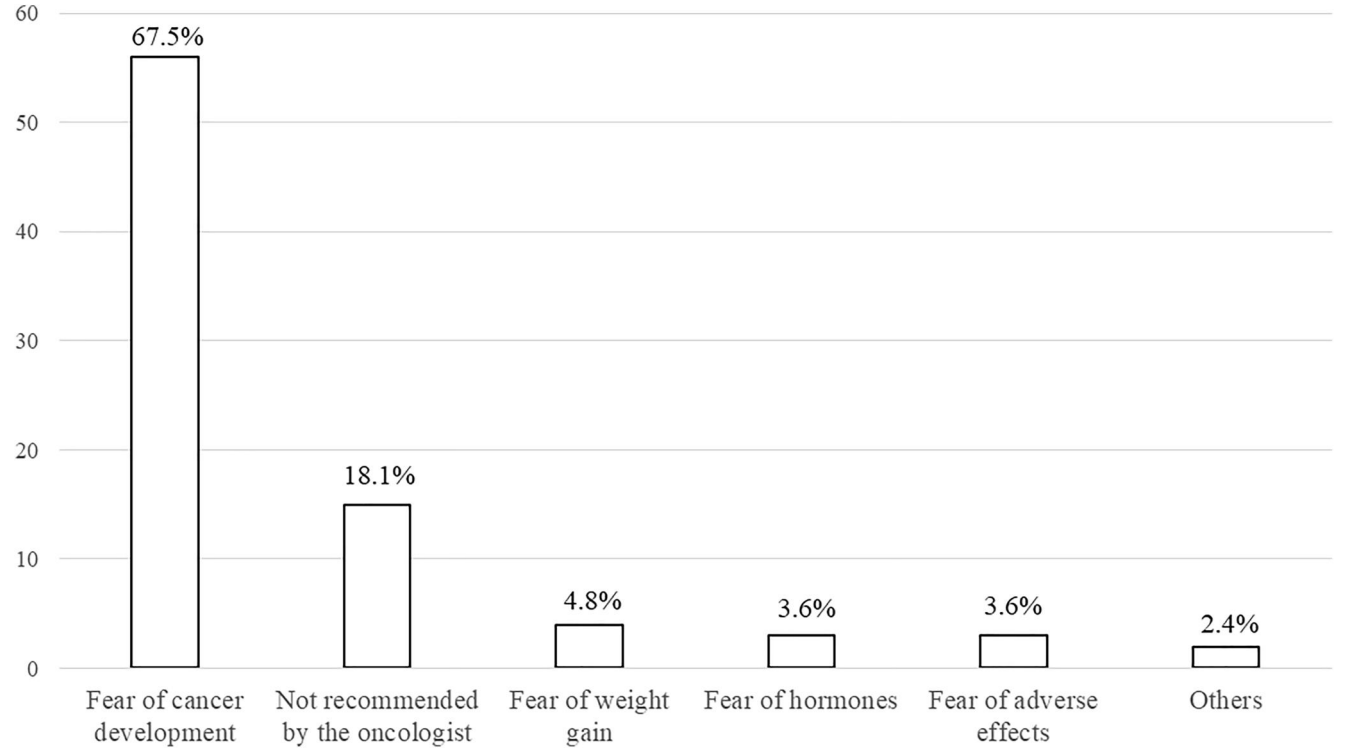

FIGURE 1 Most important concerns and fears (%) in relation to postmenopausal hormone therapy use reported by BRCA mutation carriers

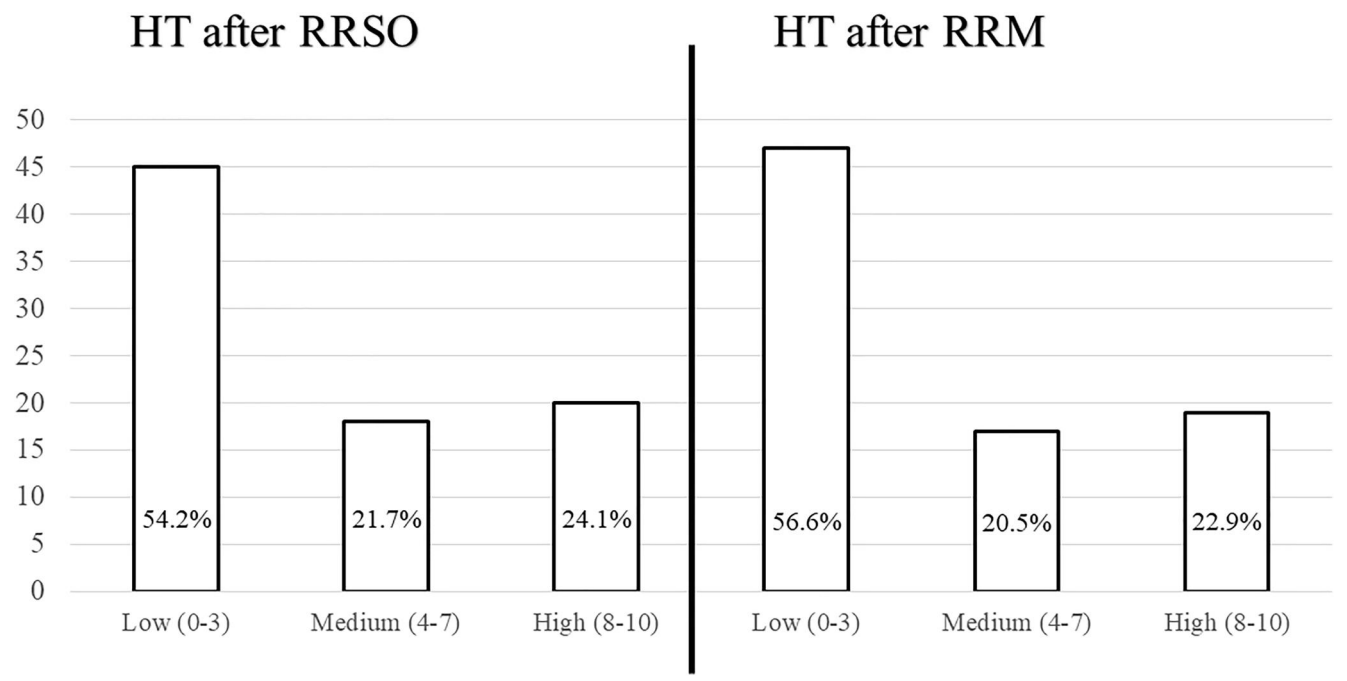

FIGURE 2 Willingness to take postmenopausal hormone therapy (HT) after undergoing risk-reducing surgeries in BRCA mutation carriers (visuo-analogic scale [VAS] from 0 to 10 [0 = very insecure, 10 = very safe] categorized as 0–3: low, 4–7: medium and 8–10: high). RRM, risk-reducing mastectomy; RRSO, risk-reducing salpingo-oophorectomy

should be further improved and, in daily practice, myths and taboos regarding side effects and long-term consequences of HT use on women's health need to be fully addressed. For example, these women are still not aware of the protective action of HT against colorectal cancer,[13] as demonstrated in another Italian trial for combined hormonal contraceptives (CHCs).[22] Colorectal cancer is the most frequent neoplasm in non-smokers of both sexes combined in Western countries. Oestrogens may exert an anti-tumour effect through the selective activation of pro-apoptotic signalling mediated by oestrogen receptor (ER)-β, the inhibition of inflammatory signals and modulation of the tumour microenvironment. HT use, as for CHC use, acts as a protective factor for this widespread cancer.[25] Poor knowledge of the positive effects of hormones on carcinogenic risks was recently demonstrated for CHCs, given that very few women correctly identified the potential reduction of ovarian and endometrial cancer risk for CHCs.[26] The cancer potential associated with HT is overestimated, especially in BRCA genetic mutation carriers, and, most importantly, for breast cancer.[17] Real numbers teach us that combined oestro-progestin therapy, particularly with synthetic progestins, is associated with an increased risk of breast cancer of 8 women per 1,000 women per 5 years. In contrast, use of oestrogens alone for less than 5 years may reduce the risk of breast cancer. Long-term oestrogen-alone therapy is associated with a very small attributable risk of ovarian cancer of 0.7 woman per 1000 women per 5 years of use.[27] This low attributable risk must however be taken into consideration in this specific very high risk population because ovarian cancer maintains a high intrinsic malignancy and high recurrence rate after surgery and first line chemotherapy.[28,29] Balanced oestro-progestin administration abrogates the effect of oestrogen and does not cause an increase in endometrial cancer. Attitudes of HCPs may contribute significantly to women's knowledge, depending on their ability to share conclusive information with potential users, especially in the hereditary cancer population.

Interestingly, less is known about the classical favourable effects on vasomotor symptoms and vaginal dryness achieved with HT use. In our study, women had a very low perception that HT can reduce vasomotor symptoms, a fact that was also reported in studies performed in a general population from Europe,[14] in Chinese women from Hong Kong[30] and from the United Arab Emirates.[13] This is surprising since the improvement of vasomotor symptoms is the best recognised and most immediate effect of HT, also in absolute terms. HT can diminish symptoms of hot flushes and vaginal atrophy in 800–900 out of 1000 users per 5 years of use, while causing only 8 extra cases of breast cancer or of venous thrombosis in the same group of women.[27] However, in our study, the perceived Likert risk is +0.1/0.2 (out of −5 to +5) for the climacteric symptoms and +0.8/1 for breast cancer and venous thrombosis.

Ultimately, we observed a better understanding of the beneficial effects of HT on the risk of bone fractures and osteoporosis as in other published trials form the general population,[16] and in contrast to a Belgian study in which osteoporosis was not perceived to be a more important disease by women with HT experience than by those without such experience.[31]

The majority of women of our population (54.6%), and also in BRCA mutation carriers, preferred the oral administration of HT. This is in line with other trials and demonstrates a higher level of compliance for oral HT formulations,[32,33] although this route of administration is associated with a greater thromboembolic risk compared to the transdermal administration.[34]

In our Institution, we have decided to treat, in accordance with oncologists and breast surgeons, all BRCA mutation carriers younger than 51 years of age after RRSO and/or premature ovarian insufficiency (POF). After 51 years of age, we commonly treat only women with important vasomotor symptoms, after the failure of alternative therapies. Oestrogen-only therapy plays a key role in hysterectomised women. In the case of an intact uterus, associations with the lowest dose of progestins/natural progesterone derivatives have to be preferred, as progestins has been shown to play an important role in BC transformation, especially in BRCA1 mutation carriers.[7] In the case of an intact uterus, associations with the lowest dose of progestins/natural progesterone derivatives have to be preferred, as progestins have been shown to play an important role in breast cancer transformation, especially in BRCA1 mutation carriers. More and better information should be given to allow to make informed decisions about their health status in menopause and the use of HT. For women requesting HT, physicians may consider informing women that climacteric symptoms may be short-lasting and benign and should be aware of the balanced effectiveness and risks of HT based on each individual situation. Unfortunately, most women with a BRCA mutation in our study reported that they would not consider taking HT even after risk-reducing surgery. However, separate data from our MFCC have shown a higher rate of actual use of HT after RRSO in women with vasomotor symptoms using our approach to counsel women with BRCA mutations.[35]

The data presented here also suggest that a specific information leaflet summarising the major benefits, risks and side effects of the HT in the context of hereditary cancer would be valuable for women at risk and doctors who care for them.

4.3 | Study limitations

There were several limitations to the survey, including its cross-sectional study design and representativeness of the sample. This is not a randomly selected population. Recruiting participants directly from the MFCC and other gynaecological hospital services might have biased the sample by including participants with relatively high health beliefs and those who are better motivated to co-operate with HCPs in screening policies. Moreover, our sample size calculation was able to recognise a true difference in the form of 0.5 units in some Likert Scale values between different groups, BRCA mutation carriers versus controls. However, it would be not large enough to enable the possible detection of negligible differences <0.5 points between different groups. Furthermore, power calculations were not helpful in the sub-analysis about knowledge of effects of HT on cancer development because we later removed the cancer survivors as they might have

overestimated the oncological risks related to HT. Ultimately, women in the younger age range were not included in the analysis despite the need to clarify the issues in relation to hormonal contraceptives in this group. However, a study is currently ongoing which focusses on this important group and data will be reported in due course.

The strengths of this study include the presence of a control group without a genetic mutation, the in-depth queries in our questionnaires and the availability of large amounts of data from participants. Moreover, the age distribution between the two included groups was similar.

5 | CONCLUSIONS

Knowledge of the possible beneficial effects of HT is relatively low in BRCA mutation carriers, as in the general population, and they are likely to overstate its negative effects and underestimate its health benefits. More and better information should be given to these high-risk women to allow them to make informed decisions about the use of HT, especially before undergoing risk-reducing surgeries.

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CONFLICT OF INTEREST

Nothing to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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