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ORIGINAL ARTICLE

BRCA carriers after risk-reducing bilateral salpingo-oophorectomy: menopausal hormone therapy knowledge gaps, and the impact of physicians' recommendations

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ABSTRACT

Objective: Female carriers of BRCA1/2 gene mutations are at an increased lifetime risk for breast and ovarian cancers. They are recommended to undergo risk-reducing surgery, including bilateral salpingo-oophorectomy (RR-BSO), upon completion of childbearing. RR-BSO surgery decreases morbidity and mortality but results in early menopause. Menopausal hormone therapy (MHT) is under-utilized despite being shown as safe for carriers. We aim to evaluate the factors associated with decision-making regarding MHT use following RR-BSO in healthy BRCA mutation carriers.

Methods: Female carriers aged <50 years who underwent RR-BSO and were followed in a multidisciplinary clinic completed online multiple-choice and free-text questionnaires.

Results: A total of 142 women met the inclusion criteria and filled the questionnaire: 83 were MHT users and 59 were non-users. MHT users underwent RR-BSO earlier than non-users (40.82 ± 3.91 vs. 42.88 ± 4.34; $p < 0.0001$). MHT usage was positively associated with MHT explanation (odds ratio 4.318, 95% confidence interval [CI] [1.341–13.902], $p = 0.014$), and knowledge regarding the safety of MHT and its effects on general health (odds ratio 2.001, 95% CI [1.443–2.774], $p < 0.0001$). MHT users and non-users retrospectively evaluated their comprehension of RR-BSO consequences as significantly lower than before surgery ($p < 0.001$).

Conclusion: Post-RR-BSO outcomes, including the effects on women's quality of life and its possible mitigation through MHT use, need to be addressed pre surgery by healthcare providers.

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Introduction

Women with an inherited mutation in the BRCA1/2 genes have an increased lifetime risk of developing breast and ovarian cancer [1]. BRCA carriers are recommended to undergo risk-reducing surgery, including bilateral salpingo-oophorectomy (RR-BSO), between ages 35 and 40 years for BRCA1 and 40–45 years for BRCA2, or upon completion of childbearing [2]. RR-BSO has been shown to reduce morbidity and mortality; however, it results in early menopause [3,4].

In the general population, women who underwent surgical menopause prior to age 45 years and did not use menopausal hormonal therapy (MHT) were found to have increased mortality compared to women who preserved their ovaries [5,6]. Early surgical menopause also significantly affects women's quality of life, with symptoms such as hot flashes, sleep disturbances and adverse effects on cardiovascular, cognitive and sexual functions [7]. Previous studies have shown that the use of MHT following RR-BSO is effective in treating and alleviating menopausal symptoms such as hot flashes and has a positive effect on cardiovascular disease, osteoporosis, depression, anxiety and cognitive function [8,9]. Therefore, MHT is recommended for women with early surgical menopause [10].

In the general population, combined estrogen–progestin menopausal hormone therapy (MHT) in postmenopausal women has been previously shown to increase breast cancer risk following 5 years of use: relative risk 1.26 (95% confidence interval [CI] [1.00–1.59]) in the Women's Health Initiative (WHI) randomized controlled trial [11] and relative risk 2.00 (95% CI [1.88–2.12]) in the Million Women Study [12]. The outcome of these results was a decline of MHT use. However, these studies included older women who used MHT following natural menopause, which might not apply to early surgical menopause following RR-BSO. The risk of developing breast cancer associated with MHT for BRCA carriers following RR-BSO remains unclear. Retrospective studies and a meta-analysis did not show an increase in the risk of breast cancer following RR-BSO in BRCA mutation carriers [9,13]. Lower risk of breast cancer incidence was related

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to estrogen treatment alone compared to combined estrogen–progestin treatment [14,15]. In a recent study of more than 300 BRCA carriers after RR-BSO who were followed for at least 7 years, MHT did not affect the overall breast cancer rate, especially when MHT was initiated before age 45 years [16]. Therefore, several guidelines have recommended the use of MHT until age 45–50 years for healthy BRCA mutation carriers following RR-BSO [10,14]. Despite the reassuring data, MHT use following RR-BSO is highly variable, reported as between 6% and 82% [17,18]. Most studies regarding decision-making in BRCA carriers have addressed decision-making pertaining to risk-reducing surgeries [19,20]. However, little is known about the factors affecting MHT use following RR-BSO. Recently, an Italian study addressing women's knowledge on the effect of MHT found their knowledge to be lacking as regards the advantages of MHT on a woman's general health, and 67% of the patients were worried that MHT would increase their oncologic risk [21].

Given the under-utilization and high variability of MHT use, despite its considerable benefits in women with surgically induced menopause, we aimed to evaluate the factors associated with decision-making regarding MHT use following RR-BSO in BRCA mutation carriers without a history of breast cancer.

Methods

Healthy women with an inherited BRCA1/2 mutation are followed in a multidisciplinary one-stop clinic at Shaare Zedek Medical Center Jerusalem, Israel. Women attend the clinic biannually following genetic diagnosis. Ovarian cancer surveillance includes a pelvic ultrasound and serum CA125 blood test, as well as breast cancer screening including breast ultrasound, mammogram and magnetic resonance imaging. Additional imaging or follow-up is performed as necessitated. In addition, women are counseled regarding risk-reducing surgeries, with a recommendation for RR-BSO following completion of childbearing at age 35–40 years for BRCA1 and 40–45 years for BRCA2 mutation carriers. While MHT use was not routinely discussed, it was addressed upon women's request prior to surgery or thereafter. Patients are recommended to continue surveillance following surgery.

All women attending the multidisciplinary clinic (MDC) were contacted by email, including an attached questionnaire with an embedded informed consent. Inclusion criteria were RR-BSO prior to menopause and age $\geq$50 years. Exclusion criteria were RR-BSO following menopause, ovarian cancer diagnosis during RR-BSO and breast cancer diagnosis prior to RR-BSO. For the purpose of this study, we defined MHT as systemic estrogen alone or combined estrogen–progestin treatment administered orally or transdermally. Vaginal estrogen was not considered MHT since it does not result in sustained estrogen levels exceeding the normal menopausal range and is not indicated for systemic menopausal symptom treatment or disease prevention [22].

The questionnaire (Supplementary data 1) included three sections, which contained multiple-choice questions and the option of free-text comments:

- Part I: clinical information included sociodemographic characteristics, reproductive and obstetric history, general health, mutation type, and family and personal history of cancer, including subsequent therapies.
- Part II: MHT use included the type of counseling received prior to surgery and the perceived degree of understanding of menopausal effects before and in retrospect, and was assessed by the Likert scale (very low = 1 to very high = 5). Type of MHT used, number of regimens and factors affecting use or discontinuation of treatment were reported. Knowledge regarding the menopausal effect on general health and effects of MHT were assessed by agreement or disagreement with statements regarding MHT.
- Part III: menopause effect was assessed by the Menopause Specific Quality of Life Questionnaire (MENQOL) questionnaire [23] with additional questions regarding sexual function.

The study was approved by the local ethics committee (# 326-20 SZMC).

Study data were collected and managed using REDCap electronic data capture tools hosted at Shaare Zedek Medical Center, Jerusalem, Israel.

Statistical analysis

The association between categorical variables was assessed using χ^2 or the Fisher exact test. The relationship between categorical and continuous variables was evaluated using the Student *t*-test or Mann–Whitney test. A paired *t*-test compared participants' understanding before surgery and in retrospect. A multivariable logistic regression model was conducted to assess independent factors associated with MHT use. All tests were two-sided. $p < 0.05$ was considered statistically significant. Analyses were carried out using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA).

Results

In total, questionnaires were sent to all 453 women aged older than 35 years followed up in the MDC, and were completed by 288 women (63.6% response rate). Out of which, 145 underwent RR-BSO and met the inclusion criteria. Three women did not state their MHT status and were excluded. Seventeen women (11.9%) did not answer the section in the questionnaire regarding decision-making, MHT use and menopausal symptoms. Age at RR-BSO ($p = 0.57$), current age (0.19), body mass index (0.74), type of BRCA mutation (0.813) and marital status (0.271) did not differ between women who completed the questionnaire and those who did not.

Sociodemographic and clinical characteristics

MHT use was reported by 83 (58.4%) women, while 59 (41.6%) were non-users. At the time of the survey, the mean age of women ever using MHT (past or present use) was significantly lower than that of non-users (46.59 ± 6.73 vs. 53.26 ± 8.39, $p < 0.0001$). In addition, women using MHT were

younger at RR-BSO (40.82 ± 3.91) compared to non-users (42.88 ± 4.34; $p < 0.0001$), and more women were younger than age 45 years at the time of surgery in the MHT user group (75 [90.3%] vs. 42 [71.1%], $p < 0.0001$). The groups did not differ regarding marital status, religious status and education level. In addition, no difference was observed in background medical conditions, previous surgeries, including risk-reducing mastectomy, and BRCA mutation type (Table 1).

Psychosocial factors affecting MHT use

Most MHT users (73.5%) reported receiving guidance regarding MHT use, at the time of their surgery, compared with 36.8% of non-users ($p < 0.0001$). This guidance was given by the surgeon in 47% versus 22.8% ($p < 0.0001$) and/or by the MDC team (physician or nurse) in 45.6% versus 26.3% ($p = 0.05$) of MHT users and non-users, respectively. The guidance provided by the general gynecologist did not differ between the groups (16.2% vs. 8.8%, $p = 0.28$).

Women who used MHT had a significantly higher level of knowledge regarding the safety of MHT and MHT's positive effect on general health (mean score 3.20 ± 1.47 [range 1–5]) than non-users (mean score 1.38 ± 1.61, $p < 0.0001$).

Overall, all participants retrospectively perceived their pre-surgery understanding of the implications of RR-BSO as significantly lower than they perceived it at the time of surgery, with no difference between users and non-users (paired *t*-test within groups, $p < 0.001$; between groups, non-significant). Both MHT users and non-users were content with their decision regarding MHT use (3.91 ± 1.31 vs. 3.68 ± 1.35, $p = 0.48$ for users and non-users [range 1–5]). Women in both groups rated their shared decision-making with their doctor regarding MHT similarly (3.3 ± 1.34 vs. 3.0 ± 1.41, $p = 0.185$ [range 1–5]).

MENQOL scores did not differ between the groups (Table 2).

The main reasons reported for MHT use

The main reasons for MHT use were recommendation of the attending physician ($n = 46$, 67.6%), menopausal symptoms ($n = 29$, 42.6%), fear of the onset of menopausal symptoms ($n = 29$, 42.6%), fear of the effect on bone density or heart disease ($n = 28$, 41.2%) and fear of aging ($n = 21$, 30.9%). The sum of answers exceeds 100% since women could choose more than one answer.

Table 1. Characteristics of the study population.

Parameter	*MHT users* (n = *83*)	*MHT non-users* (n = *59*)	p-*Value*
Demographic data			
Age (years), mean ± SD	46.59 ± 6.73	53.26 ± 8.39	0.000
Age at BSO (years), mean ± SD	40.82 ± 3.91	42.88 ± 4.34	0.000
Body mass index	26.24 ± 5.37	27.04 ± 5.35	NS
BSO at age <45 years, *n* (%)	75 (90.3%)	42 (71.1%)	0.002
Marital status, *n* (%)			
Single	2 (2.4%)	3 (5.1%)	NS
Married	75 (90.3%)	52 (88.1%)	
Separated/divorced	4 (4.8%)	2 (3.4%)	
Widower	2 (2.4%)	2 (3.4%)	
Level of education, *n* (%)			
Elementary school	1 (1.2%)	0	NS
High school	8 (9.6%)	8 (13.5%)	
Vocational school	2 (2.4%)	5 (8.5%)	
University	72 (86.7%)	46 (77.9%)	
Religious status, *n* (%)			
Secular	38 (45.8%)	22 (37.3%)	NS
Traditional	5 (6.0%)	8 (13.5%)	
Religious	21 (25.3%)	22 (37.3%)	
Ultraorthodox	4 (4.8%)	4 (6.7%)	
General health and lifestyle, *n* (%)			
Physical exercise	53 (63.8%)	33 (55.9%)	NS
Sexually active	53 (63.8%)	34 (57.6%)	0.023
Diabetes	1 (1.2%)	2 (3.4%)	NS
Hypertension	2 (2.4%)	5 (8.5%)	NS
Thrombophilia	0	0	
Other	5 (6.0%)	7 (11.9%)	NS
Any past use of hormonal contraception, *n* (%)	74 (89.1%)	44 (74.6%)	NS
Risk-reducing mastectomy, *n* (%)	26 (31.3%)	11 (18.6%)	NS
Previous surgeries, *n* (%)	24 (28.9%)	15 (25.4%)	NS
Surgical menopause, *n* (%)			
BSO only	70 (84.3%)	49/59 (83.0%)	NS
Hysterectomy + BSO	13 (15.6%)	10 (16.9%)	
Reason for BRCA testing, *n* (%)			
Known family mutation	51 (61.4%)	27 (45.7%)	0.04
Genetic study	3 (3.6%)	2 (3.4%)	
Significant family history	14 (16.9%)	23 (38.9%)	
Gene mutated, *n* (%)			
BRCA1	42 (50.6%)	29 (49.1%)	
BRCA2	36 (43.3%)	27 (45.6%)	NS
BRCA1 + 2	0	1 (1.7%)	

BSO, bilateral salpingo-oophorectomy; MHT, menopausal hormone therapy; NS, not significant; SD, standard deviation.

Table 2. Comparison of factors effecting decision-making in MHT users and non-users.

	MHT users (n = *68*)	*MHT non-users* (n = *57*)	p-*Value*
Any explanation regarding MHT[a], *n* (%)	50 (73.5%)	21 (36.8%)	0.000
Explanation by surgeon, *n* (%)	32 (47.0%)	13 (22.8%)	0.000
Explanation by MDC doctor or nurse, *n* (%)	31 (45.6%)	15 (26.3%)	0.05
Explanation by general gynecologist at HMO, *n* (%)	11 (16.2%)	5 (8.8%)	NS
Other or do not recall, *n* (%)	4 (5.9%)	2 (3.5%)	NS
To what extent did you understand the meaning of BSO prior to surgery? Mean ± SD	3.98 ± 1.05	3.94 ± 1.10	NS
In retrospect, to what extent did you understand the implication of BSO? Mean ± SD	3.38 ± 1.36	3.47 ± 1.34	NS
Paired *t*-test of BSO understanding prior to and retrospect	***p* = 0.0001**	***p* = 0.0002**	
Decreased libido (range 1–5)	2.91 ± 1.51	3.09 ± 1.48	NS
To what extent were you content with your decision regarding MHT? (Range 1–5)	3.91 ± 1.31	3.68 ± 1.35	NS
To what extent did you feel that your doctor shared with you in the decision regarding MHT? (Range 1–5)	3.30 ± 1.37	3.00 ± 1.41	0.185
Knowledge regarding MHT total score	3.20 ± 1.47	1.38 ± 1.61	0.0001
Score > 3	45 (66.2%)	11(19.3%)	0.0001
MENQOL vasomotor, mean ± SD	0.7 ± 1.31	1.23 ± 1.84	NS
MENQOL physical, mean ± SD	1.37 ± 1.19	1.53 ± 1.28	NS
MENQOL psychological, mean ± SD	1.36 ± 1.14	1.43 ± 1.24	NS
MENQOL sex, mean ± SD	2.01 ± 1.92	2.30 ± 2.19	NS
MENQOL total, mean ± SD	1.37 ± 1.01	1.53 ± 1.21	NS

[a]Any explanation: given by either the surgeon, MDT doctor, MDT nurse, general MDC or other.
BSO, bilateral salpingo-oophorectomy; HMO, health maintenance organization; MDC, multidisciplinary clinic; MENQOL, Menopause Specific Quality of Life Questionnaire; MHT, menopausal hormone therapy; SD, standard deviation.

The main reasons reported for not using MHT

The main reasons for no MHT use were fear of cancer ($n = 19$, 33.3%), medical recommendation ($n = 14$, 24.6%), lack of symptoms ($n = 13$, 22.8%), fear of side effects ($n = 9$, 15.7%), use of alternative treatment ($n = 6$, 10.5%) and medical reason ($n = 5$, 8.8%).

Reasons for discontinuation of MHT

The main reasons for discontinuation of MHT ($n = 11$) were fear of breast cancer ($n = 4$, 3.6%), side effects ($n = 4$, 3.6%), medical recommendation ($n = 2$, 1.8%), diagnosis of breast cancer ($n = 1$, 0.9%), bleeding ($n = 1$, 0.9%) and two women (1.8%) who felt that they did not need treatment any longer.

Multivariable predictors for MHT use

We performed multivariate analysis for MHT use, including age <45 years at the time of RR-BSO, knowledge score, any explanation on MHT use prior to the operation and whether the women are sexually active or not. Complete data were available for 91 women. The main significant finding was that any explanation given to the women had a positive effect on MHT use (odds ratio 4.318, 95% CI [1.341–13.902], $p = 0.014$). Additionally, knowledge regarding the safety of MHT and its impact on general health was positively associated with MHT use (odds ratio 2.001, 95% CI [1.443–2.774], $p < 0.0001$).

Open-ended questions regarding the RR-BSO experience

To allow women to discuss their experiences using their own words and bring up whatever issues matter the most to them, we asked several open-ended questions.

The first question was 'What is important for you to say to women about to undergo a risk-reducing surgery?'.

Sixty-two percent of our cohort (88 participants) responded to this question, raising eight issues (Table 3, presented in descending order). Overall, their responses reflected positive views of the procedure, primarily as a means of preventing ovarian cancer and encouraging other women to undergo surgery, with slightly fewer negative views of the hardships around the procedure, predominantly the side effects of entering menopause.

We also asked 'Is there anything else on the subject of risk reduction surgery which you would like to share with us?'.

About a third of the women ($n = 54$, 38%) answered this question. Overall, the majority highlighted difficulties of early menopause, recommending that implications of RR-BSO be discussed ahead of time. Participants mentioned side effects – physical, mental and sexual – and revealed a lack of agreement among healthcare professionals concerning MHT use. These responses demonstrate the considerable degree to which women's needs regarding the surgery go beyond ovary removal and achieving full recovery. Women reported needing information before the surgery as well as afterward. In particular, women reported how little their doctors knew of side effects and health issues; for example, the connection between heart conditions and surgical menopause (Table 3).

Discussion

Our study highlights several factors predicting MHT use, including younger age at surgery, possibly because the deleterious health consequences of the surgery are more prominent at a younger age for BSO. Younger age will probably affect the caring physician encouraging MHT use and younger women choosing to use MHT. Multivariate analysis reveals that medical recommendations for MHT use as well as higher knowledge levels regarding the safety of MHT use and its positive effects on general health are associated with greater MHT use, possibly allowing women to choose MHT treatment with greater confidence. That said, women – regardless of their MHT usage – retrospectively evaluated their pre-operational knowledge of the effects of BSO as lower than what they felt it was at the time.

Understanding the factors associated with MHT use in BRCA mutation carriers undergoing RR-BSO is essential for

Table 3. Summary of patients' responses to the question 'What do you think women should know prior to risk-reducing surgery?'.

Issue (n, %)	*Examples (verbatim/translated from Hebrew)*
Operation for prevention (23, 24%)	Best to remove rather than live in fear of dying because of remaining ovaries
	It is important to do, and the benefit outweighs the fear
Menopause	You gain a ton of weight
General and MHT (22, 23%)	You must consider that you will immediately go into menopause
	Be aware that you should take MHT
Encouraging others to do it (14, 15%)	I am grateful that I was advised to undergo the surgery
	It is the right thing to do. You are a hero
	I recommend it
Other (12, 13%)	To understand the true implications
	Ask a lot of questions
Menopause	Receive sexual counseling immediately! And have the husband be a full
Sex life (7, 7%)	partner in understanding the implication on the sex life
	There is sex life after[a]
Fertility (7, 7%)	Freeze eggs beforehand
	Make sure you are done having children
Difficult process (4, 4%)	Recovery is a bit longer than what they tell you, but entirely doable
	Prepare for changes and difficulties
Medical info (3, 3%)	Have it done laparoscopically, it is an easier recovery
	Have follow-up with a specialist after surgery
	In hindsight I would also remove the uterus to prevent cancer there
Recommend it (12, 21%)	It has been 11 years since I had my ovaries and tubes removed (after family completion) There is nothing to fear, I am not on hormones, living a good, ordinary life overall, and mainly am here to share with you
Side effects (12, 21%)	Nobody prepared me for such difficult side effects post surgery, for a decrease in quality of life, and if it was not for my online searches meant to understand the phenomenon and to connect the surgery to severe arthritis, I would not have known of appropriate MHT. I was stunned by the number of HCPs, surgeon, hospital nurses, and OB/GYNs who do not know to what degree the surgery can affect women
Medical disagreement on MHT (11, 19%)	It is unclear how hormones affect the risk of having cancer. It is hard to get hormones, and hormonal consultation
Find out all implications ahead of time (11, 19%)	After the surgery I felt a sharp decrease in sexual desire. This had not been discussed with me, and I think it should be discussed with women before ovary removal. I cannot help but think that there is a perception that women's sexual enjoyment is less of a priority than other values
Other (10, 17%)	Mental support is required throughout the decision-making process and post surgery, regarding fear of risks, self-image, body-image and femininity
Medical issues (7, 12%)	The option of hysterectomy was not mentioned, and neither was the issue of the risk in keeping the uterus

Of our respondents, six women mentioned two issues. Therefore, we calculated percentages from the total number of responses, $n = 94$. [a]This was the only positive comment regarding sex life. MHT, menopausal hormone therapy; HCPs, health care providers; OB/GYNs, Obstetricains, Gynecologists.

improving women's quality of life and general health. Furthermore, addressing these factors might help women concerned with the effects of early menopause and therefore reluctant to proceed with risk-reducing surgery. Thus, MHT and knowledge of its risks and benefits affect both quality of life and longevity.

A previous descriptive qualitative research study aimed to identify perspectives and factors associated with decision-making in women undergoing early surgical menopause. Their study included BRCA carriers as well as women who underwent BSO for other benign indications. Participants expressed that their experience prior to surgery was worse than expected and noted that they did not receive adequate support to prepare themselves to make decisions regarding therapy. Women expressed the need to learn more about symptoms of early menopause, treatment options and support resources prior to surgery. Women felt they had to be self-advocates and seek support within the healthcare system. Interestingly, 30% of the patients in the study were BRCA carriers who emphasized that they received conflicting data regarding the breast cancer risk associated with MHT use [24].

Bilateral mastectomy rates were not significantly different between the MHT users and non-users, but a larger proportion of the MHT users underwent bilateral mastectomy (31.3% vs. 18.6%). It is possible that mastectomy affected the medical recommendation toward MHT use. However, the relatively low rate of mastectomy in both groups limited the possibility to accurately assess its effect on MHT use.

Additionally, a review assessed factors associated with MHT use and decision-making following surgical menopause. Although indication for surgery was not stated, the report identified younger age, level of education, higher income and adopting lifestyle behaviors as affecting MHT decision-making following early surgical menopause. Internal factors affecting decision-making were described as mostly perceptions, beliefs and values associated with MHT, as well as knowledge and experiences with MHT. External factors included physician's recommendations and information sources [25]. It is therefore important to give the patient coherent data on MHT use prior to surgery to improve uptake of MHT treatment. Interestingly, we found that, in retrospect, women realized that their pre-surgery knowledge on the implications and side effects of the surgery was insufficient. Prior to surgery, women did not consider themselves lacking knowledge, so they did not probe their physicians for more information. These findings dovetail with research exposing that women's retrospective assessment of what they knew of

giving birth was substantially lower than how informed they felt they were prior to the delivery [26]. This consistent trend implies that patients may be unaware that they lack information, and not actively seek it.

The importance of a physician's recommendation is consistent with previous studies, as it has been described as an essential factor in decision-making regarding MHT use, and likewise affects decision-making regarding risk-reducing surgeries in BRCA carriers [27].

Furthermore, in a cross-sectional study of postmenopausal women evaluating factors associated with MHT use in the general population, the decision for MHT use was influenced by the physicians' specialty, with gynecologists preferring MHT use compared to family physicians who did not favor MHT use [28].

Although MHT use following RR-BSO was not found to increase breast cancer risk in retrospective and longitudinal studies and in meta-analysis, patients and caregivers might still be reluctant to use MHT for safety reasons, as stated previously. Therefore, emphasizing the importance of updating physicians and counseling patients prior to and following surgery is imperative. Expectations regarding menopausal symptoms and MHT use should be addressed in specialized clinics with follow-up and monitoring of long-term outcomes [29].

In light of previous studies and our results, it is clear that a physician's recommendation, including the gynecologic surgeon, is a powerful determinant, and failure to discuss treatment options in any detail may be perceived as an indirect recommendation against treatment [25]. Our finding emphasizes the need for the physician to discuss MHT safety and its importance for women's health and well-being.

Our MENQOL results did not show a difference between MHT users and non-users. A review assessing the quality of life following RR-BSO found that MHT use improved quality of life, alleviating vasomotor symptoms. However, the improvement of sexual function with MHT is inconsistent. MHT decreased pain and discomfort, while other aspects of sexual activity did not show improvement [30]. Therefore, sexual function should be addressed separately from MHT use.

Our study has several strengths. First, although this study was performed in a single MDC, patients attend the clinic from all over the country and undergo surgery in different medical centers by various physicians. These factors increase the diversity of our population. Similarly, our high response rate (89.1% of eligible patients) suggests no selection bias or response bias. These two factors contribute to the generalizability of our findings.

Our study has several limitations, primarily its retrospective nature. On average, the participants had RR-BSO surgery 11.6 years before the survey. The information is based on recollection, with symptoms and perceptions that might have changed over time. In addition, women filled out the questionnaire only after or during MHT use. Therefore, their MENQOL results represent their symptoms while on MHT treatment, with no baseline for comparison.

Limitations notwithstanding, our work highlights the under-utilization of MHT in RR-BSO women (only 54.6% of women), despite its considerable benefits. It also emphasizes the role that physicians, and surgeons have in recommending MHT to these women. Educating physicians and patients regarding the safety and general health benefits of MHT use is important and may increase patients' uptake of MHT use and preserve their general health and well-being.

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