



# Risk factors for weight gain after risk reducing salpingo-oophorectomy in premenopausal patients with hereditary ovarian cancer risk

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## ABSTRACT

**Introduction:** This study examines weight changes in premenopausal patients following risk-reducing salpingo-oophorectomy (RRSO) and factors associated with postoperative weight gain.

**Methods:** We analyzed data from premenopausal patients (age  $\leq 51$  years) with pathogenic variants in *BRCA1/2*, *ATM*, *BRIP1*, *PALB2*, *RAD51C/D*, *MLH1*, *MSH2*, *MSH6*, or *PMS2* who underwent RRSO between 2009–2016. We defined postoperative weight gain as  $\geq 5\%$  increase in weight within 5 years after RRSO and weight maintenance as  $< 5\%$  increase in weight or weight loss. Use of postoperative hormone replacement therapy (HRT) and referral to weight loss services were analyzed.

**Results:** 120 patients met inclusion criteria. Weight gain occurred in 44 (36.7 %) patients. There were no significant differences in demographic characteristics or comorbidities between groups. Preoperative weight and BMI were similar between cohorts. Mean postoperative weight and BMI were  $82.4 \pm 19.5$  kg and  $30.5 \pm 6.9$  kg/m<sup>2</sup>, respectively, in the weight gain cohort compared to  $73.1 \pm 20.8$  kg and  $26.8 \pm 7.3$  kg/m<sup>2</sup> in the weight maintenance cohort ( $p = 0.017$  and  $0.008$ , respectively). 33 patients (27.5 %) received referrals to weight management services or underwent weight loss interventions. Referrals to weight management services were significantly higher in the weight gain cohort after RRSO (36.4 % vs. 19.7 %,  $p = 0.045$ ). Approximately 50 % of patients used HRT after surgery with similar rates of use in those who had weight gain ( $n = 42$ , 55.3 %) and weight maintenance ( $n = 19$ , 43.2 %;  $p = 0.20$ ).

**Conclusions:** Over one third of patients experience weight gain after RRSO. Preoperative weight and BMI did not correlate with postoperative weight gain. These data highlight the need for targeted perioperative weight management in patients undergoing RRSO.

## 1. Introduction

Ovarian cancer is the second most common gynecologic cancer worldwide with a 5-year survival rate of 47 % (Lheureux, 2019). Although several factors contribute to the risk of developing ovarian cancer, hereditary risk plays a significant role, accounting for approximately 20–25 % cases of ovarian cancer (Minion, 2015). Patients who carry pathogenic variants or likely pathogenic variants (PV/LPV) in

*BRCA1* or *BRCA2* genes are recommended to undergo premenopausal risk reducing salpingo-oophorectomy (RRSO) to mitigate ovarian cancer risk (Liu, 2022).

The decision to undergo RRSO is complex and requires patients to consider the immediate and long term effects of the loss of ovarian function, including osteoporosis, cognitive decline, and genitourinary syndrome of menopause (Faubion, 2015). Additionally, estrogen deficiency in menopause is associated with cardiometabolic effects,

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including altering lipid metabolism, energy consumption, and increased abdominal and visceral fat (Opoku, 2023). The natural menopausal transition is associated with increased rates of obesity, but changes in weight are not well described in premenopausal patients undergoing RRSO.

A prospective study by Gibson et al. demonstrated that premenopausal patients, defined by at least one menstrual cycle in the last 3 months, undergoing hysterectomy and bilateral salpingo-oophorectomy have accelerated weight gain of 0.21 kg/m<sup>2</sup> per year in comparison to hysterectomy with ovarian conservation (0.13 kg/m<sup>2</sup> per year) or natural menopause (0.08 kg/m<sup>2</sup> per year) (Gibson, 2013). On the other hand, a questionnaire-based study by Kotsopoulos et al. demonstrated that women with a PV/LPV in *BRCA1* or *BRCA2* did not experience increased rates of weight gain following RRSO. However, this study did not stratify participants by menopausal status (Kotsopoulos, 2018). The prospective “WHAM” (What Happens After Menopause) study by Hickey et al. similarly compared premenopausal patients 12 months after RRSO to patients who retained their ovaries, finding no differences in BMI, weight, or waist circumference after RRSO when adjusting for baseline weight (Hickey, 2021). Additionally, the use of hormone replacement therapy (HRT) after surgical menopause may influence postoperative weight gain. However, the evidence for the physical effects of HRT is overshadowed by studies focused on the risks of HRT on breast cancer risk.

Altogether, confounding data regarding weight gain after RRSO for premenopausal patients complicates preoperative counseling, making it challenging for both patients and providers to fully anticipate postoperative outcomes associated with weight. This study was undertaken to clarify the impact of RRSO on weight gain. We sought to describe patterns of weight gain or weight maintenance among premenopausal patients with increased hereditary risk for ovarian cancer who have undergone RRSO and to identify risk factors for weight gain in this population.

## 2. Methods

### 2.1. Study design

We conducted an Institutional Review Board approved retrospective cohort study of premenopausal patients with a documented hereditary risk for ovarian cancer who had RRSO at the Cleveland Clinic Foundation, Cleveland, Ohio between the years 2006–2016. Patients with PV/LPV in the following genes were included: *BRCA1*, *BRCA2*, *MLH1*, *MSH2*, *MSH6*, *PMS2*, *ATM*, *BRIP1*, *PALB2*, *RAD51C*, and *RAD51D*. Patients were excluded if their last menstrual period was > 1 year prior to surgery, their age was at least 51 years, they had a personal history of ovarian cancer, or they underwent a bilateral salpingo-oophorectomy due to suspected malignancy. Additional exclusions included patients with a history of bariatric surgery prior to RRSO, or a history of hormone receptor positive breast cancer treated with tamoxifen and/or gonadotropin releasing hormone agonists/luteinizing hormone receptor agonists.

The primary outcome of this study was to identify the incidence of weight gain, defined as  $\geq 5\%$  change in weight from pre-operative weight, or weight maintenance, defined as  $< 5\%$  change in weight from preoperative weight or weight loss, in the first 5 years following RRSO. The secondary outcome was to identify factors associated with weight gain.

### 2.2. Data collection

The electronic health record was queried to identify demographic data, including age, body mass index (BMI), race, and ethnicity. Weight at the time of RRSO and 5 years after RRSO were recorded. Medical and surgical history, including medical comorbidities, medication use, substance use, and concurrent hysterectomy at the time of RRSO were

noted. Use, dose, and route of HRT within 5 years after RRSO were abstracted from medical records. New medication use and comorbidities occurring within 5 years after RRSO were also recorded. Medications noted in both the pre- and postoperative periods were those potentially associated with weight gain, including atypical antipsychotics, gabapentin, oral antihyperglycemics, insulin, glucocorticoids, or antidepressants. The incidence of anxiety and depression diagnoses and consultation with a behavioral health provider preoperatively were documented. Patient records were screened for referrals, both preoperatively and postoperatively, for weight loss or lifestyle intervention services within our hospital system. These interventions included referrals to 1) Physical or Occupational Therapy, 2) Endocrinology, Bariatric and Metabolic Clinic, 3) dietitians within the Center for Human Nutrition 4) The Obesity and Medical Weight Loss Center, 5) The Center for Integrative and Lifestyle Medicine, 6) Women's Weight Management Program, and 7) bariatric surgery. Documentation of utilization of third-party weight loss programs, such as Weight Watchers or Noom, was also noted. All data were collected and stored in a secure REDCap database (Harris, 2009).

### 2.3. Data analysis

Approximately normally-distributed continuous measures were summarized using means and standard deviations and compared using two-sample t-tests. Continuous measures that show departure from normality and ordinal measures were summarized using medians and quartiles or frequencies and percentages and compared using Wilcoxon rank sum tests. Categorical factors were summarized using frequencies and percentages and were compared using Pearson's chi-square tests or Fisher's exact tests. All analyses were done using SAS (version 9.4, The SAS Institute, Cary, NC) and a  $p < 0.05$  was considered statistically significant.

## 3. Results

### 3.1. Patient population

Out of 163 patients screened for eligibility in the study, 120 patients met inclusion criteria. Most patients were noted to have either a *BRCA1* ( $n = 67$ , 55.8 %) or *BRCA2* ( $n = 40$ , 33.3 %) PV/LPV. The remaining patients had the following PV/LPV: *PALB2* ( $n = 1$ ), *MSH2* ( $n = 2$ ), *MLH1* ( $n = 4$ ), *MSH6* ( $n = 4$ ), *PMS2* ( $n = 3$ ). A total of 76 (63.3 %) patients underwent hysterectomy with bilateral salpingo-oophorectomy, while 44 (36.7 %) patients underwent bilateral salpingo-oophorectomy only.

### 3.2. Factors associated with weight maintenance or weight gain after RRSO

There were no statistically significant differences in median age at RRSO (44.6 [IQR: 40.0–48.9] vs. 43.9 [IQR: 39.0–47.6] years, respectively;  $p = 0.29$ ), parity ( $p = 0.81$ ), race ( $p = 0.49$ ), ethnicity ( $p = 0.70$ ), or smoking history ( $p = 0.78$ ) between weight maintenance and weight gain cohorts (Table 1). Baseline comorbidities did not differ between the two cohorts, including diabetes ( $p = 0.30$ ), cardiovascular disease ( $p = 0.31$ ), peripheral vascular disease ( $p = 0.99$ ), or pulmonary disease ( $p = 0.71$ ). Both cohorts were equally likely to have a past medical history of breast cancer (40.8 % vs. 40.9 %,  $p = 0.99$ ). Furthermore, the incidence of reported anxiety ( $p = 0.098$ ), depression ( $p = 0.68$ ) or alcohol use disorder ( $p = 0.99$ ) did not differ between the two cohorts. Of the medications potentially associated with weight gain, no statistically significant differences were noted in the preoperative or postoperative use of medications between the two cohorts including the use of antidepressants, gabapentin, diabetes medications, glucocorticoids or antidepressants (Table 1). There was no difference in the rate of behavioral health consultations between the two groups.

A total of 33 patients (27.5 %) received a referral to weight

**Table 1**

Factors associated weight maintenance or weight gain after risk reducing salpingo-oophorectomy.

Variable	Total(N = 120)	Weight maintenance (N = 76)	Weight gain (N = 44)	p-value
<b>Median age at RRSO</b>	44.4 [39.8, 48.6]	44.6 [40.0, 48.9]	43.9 [39.0, 47.6]	0.29 <sup>b</sup>
<b>Parity</b>	2.0 [1.00, 3.0]	2.0 [1.00, 3.0]	2.0 [1.00, 3.0]	0.81 <sup>b</sup>
<b>Race N (%)</b>				0.49 <sup>d</sup>
White	111 (92.5)	68 (89.5)	43 (97.7)	
Black or African American	5 (4.2)	4 (5.3)	1 (2.3)	
Asian	1 (0.83)	1 (1.3)	0 (0.00)	
Other	3 (2.5)	3 (3.9)	0 (0.00)	
<b>Ethnicity N (%)</b>				0.70 <sup>d</sup>
Hispanic/Latino	1 (0.83)	1 (1.3)	0 (0.00)	
Non-Hispanic	117 (97.5)	73 (96.1)	44 (100.0)	
Did not disclose	2 (1.7)	2 (2.6)	0 (0.00)	
<b>Comorbidities N (%)</b>				0.79 <sup>c</sup>
None	69 (57.5)	43 (56.6)	26 (59.1)	
Any	51 (42.5)	33 (43.4)	18 (40.9)	
<b>Comorbidities N (%)</b>				
Diabetes	3 (2.5)	3 (3.9)	0 (0.00)	0.30 <sup>d</sup>
Cardiovascular disease	22 (18.3)	16 (21.1)	6 (13.6)	0.31 <sup>d</sup>
Peripheral vascular disease	4 (3.3)	3 (3.9)	1 (2.3)	0.99 <sup>d</sup>
Pulmonary disease	8 (6.7)	6 (7.9)	2 (4.5)	0.71 <sup>d</sup>
Kidney disease	0 (0.00)	0 (0.00)	0 (0.00)	
Thyroid disease	15 (12.5)	8 (10.5)	7 (15.9)	0.39 <sup>c</sup>
History of stroke/TIA	2 (1.7)	1 (1.3)	1 (2.3)	0.99 <sup>d</sup>
None	59 (49.2)	36 (47.4)	23 (52.3)	0.60 <sup>c</sup>
Other	15 (12.5)	9 (11.8)	6 (13.6)	0.77 <sup>c</sup>
<b>History of Breast Cancer N (%)</b>	49 (40.8)	31 (40.8)	18 (40.9)	0.99 <sup>c</sup>
<b>Anxiety N (%)</b>	7 (5.8)	2 (2.6)	5 (11.4)	0.098 <sup>d</sup>
<b>Depression N (%)</b>	17 (14.2)	10 (13.2)	7 (15.9)	0.68 <sup>c</sup>
<b>Alcohol use disorder N (%)</b>	1 (0.83)	1 (1.3)	0 (0.00)	0.99 <sup>d</sup>
<b>Pre-operative tobacco use N (%)</b>				0.78 <sup>d</sup>
Current	2 (1.7)	2 (2.6)	0 (0.00)	
Past	33 (27.5)	21 (27.6)	12 (27.3)	
Never	85 (70.8)	53 (69.7)	32 (72.7)	
<b>Preoperative medications associated with weight gain N (%)</b>				0.58 <sup>c</sup>
Yes (any)	53 (44.2)	35 (46.1)	18 (40.9)	
None	67 (55.8)	41 (53.9)	26 (59.1)	
<b>Postoperative medications associated with weight gain N (%)</b>				0.26 <sup>c</sup>
Yes (any)	68 (56.7)	46 (60.5)	22 (50.0)	
No	52 (43.3)	30 (39.5)	22 (50.0)	
<b>Behavioral health consultation N (%)</b>				0.25 <sup>c</sup>
Yes (any)	21 (17.5)	11 (14.5)	10 (22.7)	
None	99 (82.5)	65 (85.5)	34 (77.3)	
<b>Weight management consults or interventions before RRSO N (%)</b>				0.054 <sup>d</sup>
Yes	11 (9.2)	10 (13.2)	1 (2.3)	
No	109 (90.8)	66 (86.8)	43 (97.7)	
<b>Weight management consult or intervention after RRSO N (%)</b>				0.045
Yes	31 (25.8)	15 (19.7)	16 (36.4)	
No	89 (74.2)	61 (80.3)	28 (63.6)	

**Table 1 (continued)**

Variable	Total(N = 120)	Weight maintenance (N = 76)	Weight gain (N = 44)	p-value
<b>Weight Management consult or interventions N (%)</b>				–
Endocrinology, bariatrics and metabolic health center	12 (10)	6 (7.9)	6 (13.6)	0.35
Nutrition/ Dietitian	21 (17.5)	11 (14.5)	10 (22.7)	0.25
Integrative and lifestyle medicine	4 (3.3)	2 (3.6)	2 (4.5)	0.62
Women's health weight management program	7 (5.8)	2 (2.6)	5 (11.4)	0.098
Bariatrics surgery	3 (2.5)	3 (3.9)	0 (0.00)	0.30
Other (weight watchers, Noom)	7 (5.8)	4 (5.3)	3 (6.8)	0.71
<b>Postoperative HRT use within 5 years of RRSO</b>				0.20 <sup>c</sup>
Yes	61 (50.8)	42 (55.3)	19 (43.2)	
No	59 (49.2)	34 (44.7)	25 (56.8)	

management services or underwent a weight loss intervention at some point during their care. In the preoperative period, there was no statistically significant difference in referral trends between the weight maintenance and weight gain cohort (13.2 % vs. 2.3 %;  $p = 0.054$ ). Comparatively, referrals to weight management services were significantly higher in the weight gain cohort after RRSO (36.4 % vs. 19.7 %,  $p = 0.045$ ) (Table 1).

### 3.3. Change in weight and BMI after RRSO

A total of 44 (36.7 %) patients gained weight within 5 years of undergoing RRSO. The mean overall follow-up interval was  $8.8 \pm 2.6$  years and did not significantly differ between the two cohorts. The net increase in weight was 14 % among the 44 patients who gained weight (Table 2). The remaining patients maintained or lost weight, with a net decrease in weight by 2 %. Preoperative mean weight and BMI did not differ significantly between weight maintenance and weight gain cohorts ( $75.2 \pm 22.3$  kg vs.  $72.5 \pm 16.7$  kg,  $p = 0.45$ , and  $27.7 \pm 7.9$  kg/m<sup>2</sup> vs.  $26.8 \pm 6.3$  kg/m<sup>2</sup>,  $p = 0.52$ , respectively). However, mean

**Table 2**

Change in weight and BMI after risk reducing salpingo-oophorectomy.

Variable	Total (N = 120)	Weight maintenance(N = 76)	Weight gain(N = 44)	p-value
Difference between and preoperative and postoperative weight (%)	4 ± 11	−2 ± 7	14 ± 8	<0.001 <sup>a1</sup>
Preoperative weight (kg)	74.2 ± 20.4	75.2 ± 22.3	72.5 ± 16.7	0.45 <sup>a2</sup>
Preoperative BMI (kg/m <sup>2</sup> )	27.3 ± 7.4	27.7 ± 7.9	26.8 ± 6.3	0.52 <sup>a1</sup>
Preoperative BMI groups				0.75 <sup>c</sup>
BMI < 25 kg/m <sup>2</sup>	54 (45.0)	33 (43.4)	21 (47.7)	
BMI 25–29.9 kg/m <sup>2</sup>	31 (25.8)	19 (25.0)	12 (27.3)	
BMI ≥ 30 kg/m <sup>2</sup>	35 (29.2)	24 (31.6)	11 (25.0)	
Weight 5 years after RRSO (kg)	76.5 ± 20.7	73.1 ± 20.8	82.4 ± 19.5	0.017 <sup>a1</sup>
BMI 5 years after RRSO (kg/m <sup>2</sup> )	28.2 ± 7.3	26.8 ± 7.3	30.5 ± 6.9	0.008 <sup>a1</sup>
Overall follow-up	8.8 ± 2.6	8.8 ± 2.5	8.9 ± 2.8	0.85 <sup>a1</sup>

postoperative weight and BMI were  $82.4 \pm 19.5$  kg and  $30.5 \pm 6.9$  kg/m<sup>2</sup>, respectively, in the weight gain cohort compared to  $73.1 \pm 20.8$  kg and  $26.8 \pm 7.3$  kg/m<sup>2</sup> in the weight maintenance cohort ( $p = 0.017$  and  $0.008$ , respectively). Notably, postoperative weight gain was not significantly different between patients who were normal weight (BMI < 25 kg/m<sup>2</sup>) ( $n = 21$ , 38.9 %), obese (BMI  $\geq 30$  kg/m<sup>2</sup>) ( $n = 12$ , 38.7 %) or overweight (BMI 25–29.9 kg/m<sup>2</sup>) preoperatively ( $n = 11$ , 31.4 %;  $p = 0.75$ ) (Table 2).

3.4. Postoperative interventions for weight management after RRSO

There was an overall trend toward increased weight management referrals in both groups between the preoperative and postoperative periods, with a 16-fold increase in referral in the weight gain cohorts after RRSO. Among patients who were referred to or received a weight loss intervention, the baseline preoperative weight and BMI were significantly higher than those who did not undergo a weight loss intervention ( $p < 0.001$ ) (Table 3). Similarly, postoperative weight and BMI at 5 years were significantly higher in those who sought a weight loss intervention or consult.

3.5. Postoperative HRT use and association with weight gain

Overall, half (50.8 %) of patients received postoperative HRT. There were no differences in the overall postoperative HRT use between maintenance and weight gain cohorts ( $n = 42$ , 55.3 % vs.  $n = 19$ , 43.2 %;  $p = 0.20$ ). The distribution of HRT routes and types is illustrated in Fig. 1. There was a significant trend toward increased use of systemic HRT (73.8 % vs. 100 %,  $p = 0.013$ ), including transdermal HRT (45.2 % vs. 84.2 %,  $p = 0.004$ ) in the weight gain cohort. (Table 4). In addition, there was a significant increase in use of vaginal HRT among the weight maintenance cohort, while no differences were seen in the use of both systemic and vaginal estrogen. Among the 19 patients who gained weight on HRT, 7 patients (36.8 %) received estrogen and progesterone compared to 9 patients (21.4 %) in the weight maintenance group ( $p = 0.22$ ). There was additionally no significant difference in the use of estrogen alone in either group. The median duration of HRT use did not differ between the two groups.

4. Discussion

In this retrospective cohort study of premenopausal patients who underwent RRSO at our institution, we demonstrated that the incidence of weight gain within 5 years of surgery was approximately 37 %, with a

mean increase of 14 % in weight and 4 points in BMI. Additionally, we found that around one third of patients received a referral or intervention for weight management during the study (either preoperatively or postoperatively), with an increase in pattern of referrals in the postoperative period both in patients who gained weight and in those who maintained weight. Taken together, these data underscore the importance of counseling regarding weight gain and referral to appropriate weight management services in patients undergoing RRSO.

The true rates of weight gain following RRSO are challenging to define given varying definitions of weight gain, follow-up time, and factors associated with weight gain in the postmenopausal state. Some studies, such as a prospective population-based cohort study by Kapoor et al., comparing premenopausal patients with and without RRSO note an increase in weight and BMI in the RRSO cohorts, especially in the first 4–5 years after surgery (Kapoor, 2022). Alternatively, studies indicate that although estrogen depletion leads to an increase in total body fat, the concurrent decrease in lean body mass is thought to lead to little net change in total body weight (Kapoor, 2017; Leeners, 2017; Greendale, 2019). Notably, the prospective WHAM study by Price et al. found minimal differences in not only weight but also body composition of premenopausal patients two years after RRSO in comparison to patients who did not undergo RRSO, only noting an increase in abdominal visceral adipose tissue in the RRSO population (Price, 2023). Animal studies using models that mimic the postmenopausal hormonal milieu demonstrate a decrease in central abdominal fat accumulation as well as improved insulin sensitivity after exogenous estrogen therapy, indicating a role of hormonal regulation in postmenopausal weight gain (Davis, 2012). However, HRT in prospective studies such as WHAM does not appear to impact body composition significantly (Price, 2023). Confounding factors, especially physical exercise and activity level, may have a larger impact on weight gain in the perimenopausal and postmenopausal period than estrogen levels (Harris, 2009; Kapoor, 2017). In addition, changes in body composition associated with aging and menopause, such as loss of muscle mass (sarcopenia), may have a greater impact on long-term health outcomes.

Altogether, counseling regarding weight gain requires a nuanced and multidisciplinary approach, especially in patients faced with a potentially life altering decision such as risk-reducing surgery. We noted that only 17.5 % of our patients had a behavioral health consultation during the study period, which highlights an opportunity for enhancing referrals to behavioral health services. Our study further showed an increase in referral patterns to weight management services in the postoperative period in both weight groups, while patients who gained weight were significantly more likely to be referred to weight management services. Although preoperative weight and BMI were on average not significantly higher in patients who gained weight, those who utilized weight management services had a higher preoperative weight and BMI (87.6 vs. 69.2 kg and 25.6 vs. 31.8 kg/m<sup>2</sup>), suggesting that stratification to weight loss services by preoperative weight may be a viable strategy in the perioperative period.

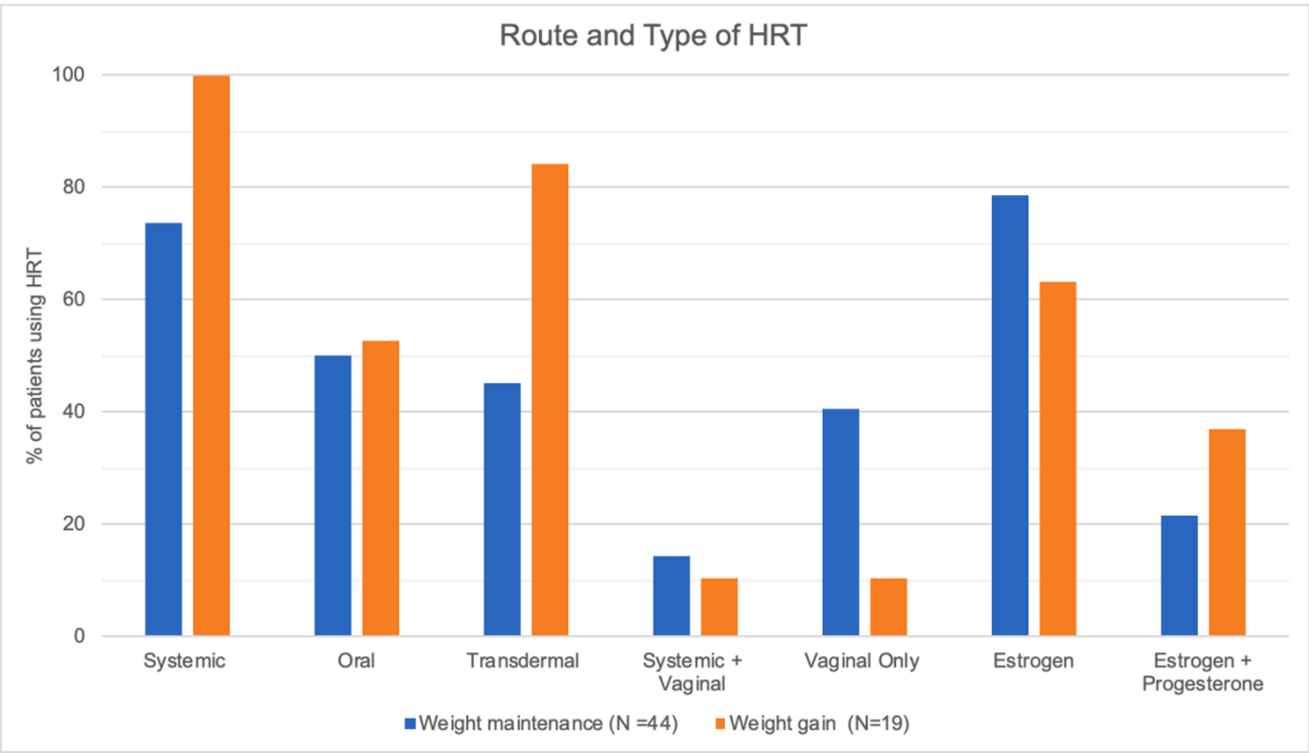
Our data also raise questions about patients' and providers' awareness of weight loss programs and highlight a missed opportunity for weight management in a population seeking care at a tertiary care center with widely available resources. Efforts to identify barriers to referral and uptake, address disparities in access to these programs, and optimize the delivery of comprehensive weight management strategies may improve post-operative outcomes and mitigate the impact of weight gain in at-risk individuals undergoing RRSO.

Data regarding the effects of HRT on weight gain after RRSO are confounding. Systemic HRT decreases vasomotor symptoms of menopause and is known to be associated with marked reduction in all-cause mortality among women who experience premature menopause, whereas low dose vaginal therapies are recommended for vulvovaginal and urinary symptoms (Faubion, 2015; Rocca, 2006). In some studies, HRT use was associated with improved postmenopausal weight regulation (Van Seumeren, 2000; Jensen, 2003). For example, in the WHAM

**Table 3**  
Postoperative interventions for weight management after risk reducing salpingo-oophorectomy.

Factor	Total (N = 120)	No weight loss consult/intervention (N = 87)	Weight loss consult or intervention (N = 33)	p-value
%Difference in weights	0.04 ± 0.11	0.04 ± 0.11	0.03 ± 0.11	0.59 <sup>a1</sup>
Pre- operative weight (kg)	74.2 ± 20.4	69.2 ± 15.0	87.6 ± 26.5	<0.001 <sup>a2</sup>
Pre-op BMI	27.3 ± 7.4	25.6 ± 5.5	31.8 ± 9.6	0.001 <sup>a2</sup>
Weight (kg) 5 years post- operatively	76.5 ± 20.7	71.8 ± 17.0	88.9 ± 24.5	<0.001 <sup>a2</sup>
BMI 5 years post- operatively	28.2 ± 7.3	26.6 ± 6.1	32.3 ± 8.7	0.001 <sup>a2</sup>





**Fig. 1.** Distribution of hormone replacement therapy routes and types. Legend: Distribution of types and routes of hormone replacement therapy used post-operatively, comparing patients with and without weight gain.(Print in color).

**Table 4**  
Postoperative hormone replacement therapy (HRT) type, route and association with weight gain.

	Total N (%)	Weight maintenance (N = 44)	Weight gain (N = 19)	p-value
HRT route				
Systemic	50 (82.0)	31 (73.8)	19 (100)	0.013
Oral	31 (50.8)	21 (50)	10 (52.6)	0.85
Transdermal	35 (37.4)	19 (45.2)	16 (84.2)	0.004
Systemic + vaginal	61 (100)	6 (14.2)	2 (10.5)	–
Vaginal only	19 (31.1)	17 (40.5)	2 (10.5)	0.019
HRT type				0.22
Estrogen alone	45 (73.8)	33 (78.6)	12 (63.2)	
Estrogen + Progesterone	16 (26.2)	9 (21.4)	7 (36.8)	
Median duration of systemic HRT (months)	53.0 (16.5, 60.0)	51.0 (19.0, 60.0)	57.0 (14.0, 60)	0.46

study by Hickey et al, 60 % of patients after RRSO initiated HRT which demonstrated a protective effect on weight circumference in comparison to those patients who did not initiate HRT (Hickey, 2021). In our cohort, only 50 % of patients received any form of HRT post-operatively. This rate is in line with other retrospective studies that report rates of HRT use in RRSO, indicating an overall low uptake of HRT in this population (Johansen, 2017; Vermeulen, 2017; Jang, 2020). Interestingly, we found that there was no significant difference in weight gain or weight loss according to overall HRT use; however, the route of HRT differed significantly between the weight maintenance and weight gain cohorts (systemic, transdermal and vaginal estrogen use). The biologic plausibility of the relationship between HRT route and weight gain or weight maintenance is limited by our small sample size and lack of data on dosing or the use of testosterone supplementation. Our findings emphasize the importance of considering individualized HRT strategies

in this population and the need to investigate the role of HRT type and route of HRT on body weight as well as body composition in future studies.

Change in body weight can have a profound impact on physical and psychological well-being and can be a component of “body image”. Several studies have demonstrated that weight gain is one of the concerns that women have after RRSO (Campfield, 2011; Bai, 2019; Hall-lowell, 2012). In a retrospective questionnaire study, Campfield et al. found that 49 % of respondents would have preferred more preoperative counseling on the impact of risk-reducing surgery on body image (Campfield, 2011; Bai, 2019). However, most data investigating the psychological impact of risk reducing surgery in patients with hereditary breast and ovarian cancer come from data in patients undergoing risk reducing mastectomy. The literature demonstrates that women who have a prophylactic mastectomy report feeling self-consciousness, less sexually attractive, and dissatisfied with their surgical scars after their surgery (Brandberg, 2008). In a prospective study of nearly 150 patients who underwent risk-reducing mastectomy, concerns with body image were found even after an average follow-up time of 11.5 (range 6.0–19.7) years after surgery, demonstrating the lasting impact of these decisions on patients’ lives (Campfield, 2011; Bai, 2019). Notably, the TUBA study, a multicenter nonrandomized controlled preference trial, comparing patients with PV in BRCA1/2 who underwent RRSO versus bilateral salpingectomy found worse menopause related quality of life scores using the Greene Climacteric Scale after salpingectomy only (Chapman, 2011; Steenbeek, 2021). However, isolating the psychological impact of RRSO as it relates to changes in weight remains challenging, and continued research in this area is warranted.

This study adds to a small body of literature that investigates the impact of RRSO on weight changes in premenopausal patients with hereditary risk for ovarian cancer. Limitations in our study include those inherent to its retrospective design which have the potential to introduce biases in our data sample and data collection. Our results relied on information documented in the medical records on patient weight,

preoperative counseling, the use of behavioral interventions and utilization of weight loss programs. Patients' individual activity levels, use of outside weight management programs, and quality of life measures, all important factors in postoperative weight management, could not be explored in our study. Our definition of weight gain included changes in weight 5 years after surgery, allowing for factors beyond surgical menopause to impact trends in weight. Furthermore, we conducted this study at a tertiary care center with access to weight management programs that are not generalizable to other institutions. The small sample size of our study and presence of missing data from our retrospective database limits our ability to draw meaningful conclusions regarding weight gain and RRSO. There is a strong unmet need for large, multi-center, prospective studies to further advance our understanding of patients' short- and long-term health outcomes in this population.

## 5. Conclusion

Patients undergoing RRSO in the setting of hereditary ovarian cancer risk must consider a variety of factors when making the decision to undergo surgery, including possible weight gain. In our cohort, over 1 in 3 women experienced weight gain within 5 years from RRSO. In order to guide preoperative counseling regarding potential weight gain after RRSO and methods to maintain weight, further research is needed to identify risk factors associated with weight gain and the impact of HRT on body composition parameters. Our findings offer opportunities for both pre- and post-operative interventions aimed at optimizing weight management after RRSO.

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## CRediT authorship contribution statement

**Surabhi Tewari:** Writing – review & editing, Writing – original draft, Methodology, Data curation, Conceptualization. **Karen Hurley:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Meng Yao:** Writing – review & editing, Formal analysis. **Snehi Shah:** Writing – review & editing, Writing – original draft. **Melissa Yurch:** Project administration, Data curation. **Anna Chichura:** Writing – review & editing. **Mariam AlHilli:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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