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Anthropometric characteristics and ovarian cancer risk and survival

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Abstract

Purpose—Multiple studies have examined the role of anthropometric characteristics in ovarian cancer risk and survival; however, their results have been conflicting. We investigated the associations between weight change, height and height change and risk and outcome of ovarian cancer using data from a large population-based case-control study.

Methods—Data from 699 ovarian cancer cases and 1802 controls who participated in the HOPE study were included. We used unconditional logistic regression adjusted for age, race, number of pregnancies, use of oral contraceptives, and family history of breast or ovarian cancer to examine the associations between self-reported height and weight and height change with ovarian cancer risk. Cox proportional hazards regression models adjusted for age and stage were used to examine the association between the exposure variables and overall and progression-free survival among ovarian cancer cases.

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Results—We observed an increased risk of ovarian cancer mortality and progression for gaining more than 20 pounds between ages 18 to 30, HR=1.36; 95% CI=1.05–1.76, and HR=1.31; 95% CI=1.04–1.66 respectively. Losing weight and gaining it back multiple times was inversely associated with both ovarian cancer risk, OR=0.78; 95% CI=0.63–0.97 for 1–4 times and OR=0.73; 95% CI=0.54–0.99 for 5–9 times, and mortality, HR=0.63; 95% CI=0.40–0.99 for 10–14 times. Finally, being taller during adolescence and adulthood was associated with increased risk of mortality. Taller stature and weight gain over lifetime were not related to ovarian cancer risk.

Conclusions—Our results suggest that height and weight and their change over time may influence ovarian cancer risk and survival. These findings suggest that biological mechanisms underlying these associations may be hormone-driven and may play an important role in relation to ovarian carcinogenesis and tumor progression.

Keywords

height; weight; height change; ovarian cancer risk; ovarian cancer survival

Introduction

Ovarian cancer accounts for only 1.3% of new cancer cases in the United States [1], at the same time being the deadliest gynecological cancer [2]. At the time of diagnosis, 60% of patients present with a distant stage for which five-year survival rate is only 28.9% [1]. Given the low survival rates among ovarian cancer patients, it is important to identify factors related to both risk and survival in order to develop measures to decrease incidence and mortality.

Findings of previous studies suggest that anthropometric characteristics may be related to ovarian cancer risk and prognosis. In fact, several pooled and meta-analyses demonstrated a link between obesity and ovarian cancer risk and survival [3–6]. Multiple epidemiological studies, individually and as a part of meta-analyses, have also shown an increased risk of ovarian cancer associated with taller adult height [4, 7–9]. The World Cancer Research Project Fund/American Institute for Cancer Research, in their Ovarian Cancer 2014 Report, concluded that the evidence for the link between adult height and increased ovarian cancer risk was convincing, and for body mass index (BMI), the evidence was probable [9, 10]. Although a large number of studies have been conducted to investigate the association between BMI and ovarian cancer survival, the role of height in ovarian cancer survival has been largely unexplored. Two of the previously conducted studies resulted in no association between height and mortality [11, 12] whereas two other studies showed an increased risk of dying among those in the higher categories of height compared to the lower categories [13, 14].

The role of the lifetime change of weight and height in relation to ovarian cancer risk and outcomes also remains unclear. Several studies conducted to examine the association between weight gain and ovarian cancer observed either an increased risk of ovarian cancer associated with weight gain [15–17] or found no association [18–20]. To our knowledge, none of the previous studies evaluated height change.

To address the inconsistency of the evidence in regards to the association between selected anthropometric characteristics and ovarian cancer, we examined the role of height and lifetime change in weight and height in ovarian cancer risk and prognosis using data from a large population-based case-control study.

Materials and Methods

Details of the study have been published previously [21, 22]. Briefly, this case-control study titled the Hormones and Prevention study (HOPE), was conducted in Western New York, Eastern Ohio, and Western Pennsylvania regions. Cases were diagnosed with ovarian, fallopian tube, or peritoneal cancer between February 2003 and November 2008. Patients were identified from hospital tumor registries, clinical practices, or pathology databases and were diagnosed within nine months of recruitment. Controls were selected via random-digit phone dialing. Both cases and controls were at least 25 years of age with no prior history of cancer.

The participants underwent extensive in-home interviews conducted by trained study personnel. The interviewers collected information on lifestyle habits, reproductive, gynecological, medical, and family history. Study participants also reported their weight at the age of 18, 30, and 50, and at the reference date, the tallest height in adulthood, height at the age of 18 and the reference date with the reference date being defined as the date nine months prior to the interview. Moreover, participants were asked how many times they lost at least 10 pounds and then gained it back and body parts where gained weight accumulates. They also reported their perceived height compared to their peers at the age of 9, 12, and 15.

For cases, additional medical information, including disease characteristics (stage, grade, histology, gross disease removal, and disease progression) and treatment information, was ascertained by medical records abstraction. Health records were collected until loss to follow up, death, or end of follow up in May, 2014. Vital status of participating cases was determined from the medical records abstraction or by searching the National Death Index and Social Security Death Index.

The study protocol was approved by the Institutional Review Boards at the participating institutions. All the women provided informed consent to participate in the study.

Statistical Analysis

Out of 902 initial cases who completed the interview, we excluded patients diagnosed with non-epithelial or borderline tumors (N=129), cases who did not undergo a standard ovarian cancer treatment regimen (surgery or chemotherapy) (N=50), those who did not have any treatment information (N=9), and those who were not followed (N=15) [23]. Our final study sample consisted of 699 cases and 1802 controls.

Using data on weight at ages 18, 30, and 50 and at the reference date, we created variables representing weight change between ages 18 and 30, and between 30 and 50. Because we did not collect the data on the weight at the time close to diagnosis and because the weight at the reference date could have been affected by cancer, we also created an additional variable

representing the most recent self-reported weight prior to diagnosis for cases and prior to the reference date for controls. This variable had the following values: for women younger than 30, the most recent weight was the weight at age 18, for those younger than 50- the weight at age 30, and for the participants older than 50- the weight at age 50. We then created another variable representing the weight change between the most recent weight and weight at the reference date. Finally, these weight change variables were categorized utilizing the same categories as the ones used by McGee et al. [24]: loss of more than 10 pounds, loss or gain within 10 pounds, gain of 10– 20 pounds, and gain of >20 pounds.

For stature, we categorized the variables representing height in cm at age 18, the tallest height in adulthood, and height at the reference date by splitting these variables into quartiles in the controls population [25] and using the same cut points in cases. We also created the variable representing height change between the age of 18 and the reference date. This variable was categorized using the following cutpoints: –5, 0, 5 cm. Moreover, we created an additional variable for the height change from 9–10 years of age to 15–16 years of age. This variable had the following categories as defined in the questionnaire: remained about the same as peers, remained much shorter, remained somewhat shorter, remained somewhat taller, and remained much taller.

Using the corresponding variables for weight and height at the different ages, we created variables representing BMI at ages 18, 30, 50, the most recent BMI prior to ovarian cancer diagnosis, and BMI at the reference date. These variables were then categorized into underweight, normal weight, overweight, and obese categories using cut points recommended by the World Health Organization[26]. We also created a variable representing BMI change over time, from age 18 until the reference date.

We used Chi-square test and Student's t-test to compare demographic, reproductive, and lifestyle characteristics and medical history between cases and controls. Comparison of important survival characteristics between those who died and those who remained alive were published earlier [23]. Using multivariate unconditional logistic regression we calculated odds ratios (ORs) and corresponding 95% confidence intervals (CIs) to evaluate the association between weight change, height, and height change and ovarian cancer risk. The models were adjusted for *a priori* identified confounders such as age at the time of ovarian cancer diagnosis, race, number of pregnancies, use of oral contraceptives, and family history of breast or ovarian cancer. Additional adjustment for other potential covariate, such as education, history of diabetes and hypertension, tubal ligation, hysterectomy, history of endometriosis, age at menarche, breastfeeding, number of live births, smoking, and physical activity did not produce a meaningful change in the ORs (more than 10% change), and, therefore, these variables were not included in the final models.

We defined overall survival (OS) as the time from the date of primary surgery to the date of death or the date of last contact [23]. Progression-free survival (PFS) was defined as the time since the date of primary surgery to the date when progression status was determined. Progression was defined as persistence, recurrence, or death. To estimate the associations between the exposures of interest and the survival outcomes, we used Cox proportional hazards models adjusted for age and stage. Similar to the analysis for ovarian cancer risk,

additional adjustment for other potential covariates such as race, history of diabetes, hypertension, and endometriosis, histology, grade, gross disease removal during primary surgery, smoking, physical activity, and the number of cycles of primary chemotherapy did not substantially impact the estimated HRs; therefore, these variables were not included in the main models.

To account for potential confounding by BMI [8], we adjusted the models assessing the associations for height at age 18, the tallest height in adulthood, and height at the reference date for BMI at the age 18, age 30, and BMI at the reference date respectively. For the weight change and times losing 10 pounds variables, we additionally adjusted each model for starting body weight.

We repeated the analysis limiting cases to high-grade serous cases only. Finally, we stratified the associations by menopausal status and hormone therapy use to examine whether these factors modified the association between height, weight, and height and weight change and ovarian cancer risk. To assess the presence of multiplicative interaction between the anthropometric characteristics and menopausal status and hormone therapy, we entered multiplicative terms between each exposure and each the potential effect modifiers into the model. We used the likelihood ratio test to assess the significance of these terms. P-values less than 0.05 were considered significant. We used the statistical software SAS 9.4 to conduct the analyses.

Results

Demographic, reproductive, and lifestyle characteristics of the cases and controls are presented in Table 1. Cases were significantly more likely than controls to be older, non-white, report no history of diabetes, no tubal ligation, no use of oral contraceptives, have hysterectomy, have a family history of breast or ovarian cancer, and report never being pregnant, have live births, or practice breastfeeding. Compared to cases who remained alive, cases who deceased during follow-up were more likely to be older, have history of diabetes, be diagnosed with advanced disease, have poorly differentiated tumors or tumors of a serous histotype, develop ascites, and experience presence of gross disease after primary surgery [23].

We observed reduced ovarian cancer risk associated with the number of times a woman lost and gained weight back (Table 2). In fact, for losing 10 pounds or more and then gaining them back, the associations were the following: for 1–4 times, OR=0.78; 95% CI=0.63–0.97 and for 5–9 times, OR=0.73; 95% CI=0.54–0.99. For losing and gaining weight more than 10 times the association was not significant. We also observed an increased risk of ovarian cancer associated with weight gain accumulating all over the body, OR=1.30; 95% CI=1.00–1.68. None of the other weight change, height, or height change variables was associated with ovarian cancer risk.

As presented in Table 3, gaining weight over time was associated with survival outcomes. Gaining more than 20 pounds between ages 18 to 30 was associated with both increased risk of mortality and progression, HR=1.36; 95% CI=1.05–1.76, and HR=1.31; 95% CI=1.04–

1.66 respectively. A more moderate weight gain, 10–20 pounds, between ages 18 to 30 was also associated with increased risk of progression, HR=1.24; 95% CI=1.00–1.54. We also observed that losing and gaining weight back multiple times was inversely associated with survival outcomes. In fact, losing 10 pounds and gaining them back 10–14 times was inversely associated with both mortality, HR=0.63; 95% CI=0.40–0.99, and progression of ovarian cancer, HR=0.61; 95% CI=0.41–0.91.

Being taller compared to peers during childhood and adolescence years was positively associated with mortality and risk of the disease progression. In fact, being much taller than the peers at 9–10 years of age was associated with higher risk of progression, HR=1.58; 95% CI=1.09–2.29. Being very tall at 15–16 years of age was also related to both mortality and progression, HR=2.19; 95% CI=1.37–3.52, and HR=2.28; 95% CI=1.45–3.58, respectively, although these results were based on a very low number of exposed women. Remaining much taller than the peers over adolescent years was also associated with increased risk of progression, HR=1.82; 95% CI=1.08–3.05.

Being tall in adulthood was also associated with increased mortality. In fact, for height at age 18, tallest height in adulthood, and height at the reference date, compared to the lowest quartile, being in the highest quartile was associated with increased risk of dying, HR=1.36; 95% CI=1.03–1.80, HR=1.39; 95% CI=1.04–1.85, and HR=1.51; 95% CI=1.17–1.94 respectively. Additional adjustment of the model assessing the associations between height and ovarian cancer risk and survival for BMI and, for the weight change and times losing 10 pounds variables, for starting body weight resulted in a very small change in the original ORs and HRs.

The observed associations between ovarian cancer risk and the weight loss and gaining it back became stronger among postmenopausal and those who reported using hormone therapy. In fact, among postmenopausal women, losing weight and gaining it back 1–4 times and 5–9 times was inversely associated with ovarian cancer risk, OR=0.69; 95% CI=0.54–0.90 and OR=0.67; 95% CI=0.47–0.96 respectively (data not shown). For premenopausal women, these associations were weaker and non-significant. Among users of menopausal hormone therapy, weight loss and gain 1–4 times and 5–9 times over lifetime was inversely associated with ovarian cancer risk, OR=0.63; 95% CI=0.45–0.88 and OR=0.57; 95% CI=0.35–0.90, respectively. At the same time, for non-users, these associations were non-significant, OR=0.91; 95% CI=0.68–1.22 for weight loss and gain 1–4 times, and OR=0.88; 95% CI=0.59–1.33 for weight loss and gain 5–9 times over lifetime. Finally, for those women whose weight in adulthood increased from underweight/normal to overweight/obese and remained overweight/obese, and reported using hormone therapy, the association was inverse but non-significant, OR=0.79; 95% CI=0.56–1.12. For women in the same weight change category who were also non-users of hormone therapy, OR was equal to 1.15; 95% CI=0.86–1.54.

We observed multiplicative interaction between the variable representing change of BMI over lifetime and use of hormone therapy, $p=0.036$. None of the other interaction terms were significant. Limiting cases to those with high-grade serous tumors did not result in a considerable change in ORs or HRs obtained in the main analyses.

Discussion

Our results suggest that height at different ages and lifetime weight change may influence ovarian cancer risk and survival outcomes. Specifically, we observed that taller height in adolescence and adulthood is associated with both OS and PFS. Similar to our results, in the study by Rodriguez et al. [14], taller height (> 177 cm) was positively, although non-significantly, associated with mortality among ovarian cancer patients, RR=1.41; 95% CI=0.95–2.09. In another study, conducted among South Korean women, it was also demonstrated that taller stature is associated with a worse survival, HR=1.29; 95% CI=1.09–1.53 for 5-cm increment in height [13]. Finally, in a large study of adult height and the risk of cause-specific deaths, height was associated with an increased risk of ovarian cancer-related deaths, HR=1.07; 95% CI=1.01–1.14 [27].

The observed association between taller height and increased risk of death could have the following explanation. Height is a surrogate for childhood or adolescence exposures [28] including exposure to certain growth factors [14]. Among these factors, insulin-like growth factor-I (IGF-I) plays a key role in promoting growth during the different stages of life [29]. Moreover, IGF-I and its binding protein, IGFBP, are also involved in follicular growth and development and steroidogenesis in the ovarian tissue [30, 31]. On the other hand, IGF-I can favor cell proliferation and inhibit apoptosis [32, 33] therefore influencing the process of cancer progression. In preclinical studies, IGF-I and its binding protein were shown to promote proliferation and invasion of ovarian cancer cells [34–36]. Moreover, IGF was shown to initiate proliferation and hyperplasia in ovarian surface epithelium in a mouse model [37]. Hence, it is likely that exposure to higher levels of IGF-I over lifetime underlines the association between taller height in adolescence and adulthood with increased risk of mortality and disease progression observed in our study.

In contrast to several other studies on height and ovarian cancer risk [7, 8, 17, 38–41], we did not observe an elevated risk of ovarian cancer associated with taller stature during either adolescence or adulthood. However, our results are similar to the ones observed by others [16, 42–45], including the most recent large prospective cohort that also resulted in no association between height and overall risk of ovarian cancer [46].

Our findings suggest that weight gain during early adulthood is associated with worse clinical outcomes. An increased risk of mortality and progression among those who reported weight gain between ages 18 and 30 and no association for weight gain later in life could indicate that accumulation of excessive weight and mechanisms associated with the weight gain are more relevant to cancer progression compared to the same processes occurring later in life.

Weight gain can impact ovarian cancer survival via metabolic processes controlled by the adipose tissue. The latter influences cancer risk and progression through its promotion of hyperinsulinemia and increased production of IGF-I [47]. Moreover, adipocytes may favor cancer progression via release of leptin which has been shown to have strong proinflammatory properties [15], to promote mitosis and angiogenesis and inhibit apoptosis [48]. Finally, increased adiposity is associated with elevating levels of C-reactive protein,

tumor necrosis factor (TNF), and various interleukins [48] which demonstrates that adiposity could influence ovarian cancer initiation and prognosis by promoting chronic inflammation [15].

In this study, we also observed that weight loss and its subsequent gain that occurred multiple times throughout life is inversely associated with ovarian cancer risk, mortality, and progression. The biological mechanisms driving these associations are unclear. Potentially, reversal of the processes underlying the link between adiposity and cancer progression can explain our results. For instance, intentional weight loss has been characterized by decrease in production of insulin, estrogen, C-reactive protein, TNF, and IL-6 [48, 49]. Some studies have also demonstrated that intentional weight loss could lead to decrease in IGF-I and IGFBPs levels, although these findings have not been confirmed in other studies [49].

To better understand our findings, it is important to take into consideration the strengths and limitations of this study. One of the strengths of this study is the availability of detailed information on weight and height throughout lifetime, including adolescence. We were also able to account for a large number of potential confounders, including factors related to both risk and survival. Other strengths relate to the availability of detailed information on clinical characteristics at diagnosis and ovarian cancer outcomes.

At the same time, there are also some limitations that need to be considered. First, despite a large number of participants in our study, we may not have had enough power to detect the association between some of the exposures and risk and survival outcomes. Second, because the data were collected via self-administered questionnaires instead of the actual measurements of anthropometric characteristics and because the reference date could have been several months prior to diagnosis, the participants may have misreported their height and weight. This error, most likely of a non-differential nature, could have resulted in attenuation of the risk estimates. Moreover, self-reported height may not have been a good proxy for the growth hormone exposure. It was suggested that leg length and sitting height could represent the growth hormone exposure better than stature in pre- and post-puberty, respectively [8, 50]. Further, selection bias might have slightly impact the results since some patients may have not been included due to severity of their disease or due to the fact that they died prior to being included in the study. Finally, for survival analysis, we were not able to account for deaths attributed to ovarian cancer. However, as it was shown in other studies [6, 51], the majority of cases, are, most likely, died of ovarian cancer.

In summary, our findings suggest that height and weight are related to ovarian cancer risk and survival. Specifically, we observed that taller height and weight gain are associated with worse prognosis, and the weight loss and its subsequent gain is inversely associated with both risk and survival. Further biological research is needed to investigate the mechanisms underlying these associations. Moreover, prospective studies may be necessary to clarify whether prediagnostic intentional weight loss is beneficial for ovarian cancer prevention and treatment.

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Table 1Selected characteristics of HOPE study cases and controls¹.

Characteristic	Cases, n=699(%)	Controls, n=1,802 (%)	p-value ²
Age at diagnosis (years), mean (SD)	59.6 (12.0)	57.0 (12.4)	<0.001
Race			
White	671 (96.0)	1758 (97.6)	0.03
Non-white	28 (4.0)	44 (2.4)	
Education			
High school or lower	306 (43.8)	617 (34.2)	<0.001
More than high school	393 (56.2)	1185 (65.8)	
History of diabetes			
No	637 (91.1)	1585 (88.0)	0.02
Yes	62 (8.9)	217 (12.0)	
History of hypertension			
No	442 (63.2)	1140 (63.3)	0.99
Yes	257 (36.8)	662 (36.7)	
Menopausal status at the time of interview			
Premenopausal	180 (25.8)	569 (31.7)	0.001
Postmenopausal	506 (72.5)	1173 (65.3)	
Unknown	12 (1.7)	55 (3.1)	
Use of oral contraceptives			
No	411 (58.8)	1272 (70.6)	<0.001
Yes	288 (41.2)	530 (29.4)	
Use of hormone replacement therapy			
No	411 (58.8)	1071 (59.4)	0.75
Yes	288 (41.2)	731 (40.6)	
Tubal ligation			
No	512 (76.2)	1162 (65.3)	<0.001
Yes	160 (23.8)	616 (34.7)	
Hysterectomy			
No	549 (78.5)	1495 (83.0)	0.01
Yes	150 (21.5)	307 (17.0)	
Family history of OVCA or BRCA			
No	545 (78.0)	1494 (82.9)	0.004
Yes	154 (22.0)	308 (17.1)	
Age at menarche			

Characteristic	Cases, n=699(%)	Controls, n=1,802 (%)	p-value ²
11	141(20.2)	444 (24.6)	0.09
12	194 (27.7)	463 (25.7)	
13	187 (26.8)	484 (26.9)	
14	177 (25.3)	411 (22.8)	
Breastfeeding			<0.001
No	312 (56.5)	692 (44.2)	
Yes	240 (34.5)	872 (55.8)	
Number of pregnancies			<0.001
0	118 (16.9)	167 (9.3)	
1	78 (11.2)	188 (10.3)	
2	170 (24.3)	458 (25.4)	
3	134 (19.2)	426 (23.6)	
4	95 (13.6)	284 (15.8)	
5	104 (14.9)	279 (15.5)	
Number of live births			<0.001
0	145 (20.7)	230 (12.8)	
1	89 (12.7)	228 (12.6)	
2	206 (29.5)	593 (32.9)	
3	137 (19.6)	418 (23.2)	
4	65 (9.3)	190 (10.5)	
5	57 (8.2)	143 (7.9)	

¹ - abbreviations used: BRCA- breast cancer, OVCA- ovarian cancer

² -p-value for t-test for age at diagnosis and Chi-square test for categorical variables

Table 2

Association between weight change, height and height change and ovarian cancer risk, HOPE study.

Variables	Cases N=699	Controls N=1802	OR (95%CI) ^I
Weight change between ages 18 to 30, pounds			
–10	55	121	1.11 (0.77–1.60)
Within 10	233	560	1.00 (ref)
10– 20	243	637	0.95 (0.76–1.18)
>20	159	452	0.90 (0.70–1.15)
Weight change between ages 30 to 50, pounds			
–10	26	49	1.15 (0.69–1.94)
Within 10	162	332	1.00 (ref)
10– 20	159	412	0.81 (0.62–1.06)
>20	202	476	0.97 (0.74–1.26)
Weight change between the most recent time period to the reference date, pounds ²			
–10	65	197	0.82 (0.59–1.13)
Within 10	264	680	1.00 (ref)
10– 20	169	447	0.94 (0.74–1.19)
>20	198	474	1.06 (0.84–1.33)
BMI change over time			
Remained normal weight	233	637	1.00(ref)
Increased from underweight/normal to overweight/obese and remained overweight/obese	242	628	1.04 (0.84–1.28)
Remained overweight/obese	56	126	1.29 (0.91–1.83)
Decreased from overweight/obese to normal	11	32	0.97 (0.48–1.97)
Body parts where gained weight accumulates			
Around the waist and abdomen	354	1009	1.00 (ref)
Around the chest and shoulders	15	27	1.72 (0.90–3.31)
Around the hips and thighs	150	355	1.25 (0.99–1.58)
Equally all over	120	270	1.30 (1.00–1.68)
Other areas	60	138	1.30 (0.93–1.82)
Times lost 10 pounds or more and gained them back			
Never	210	431	1.00 (ref)
1–4 times	312	874	0.78 (0.63–0.97)
5–9 times	85	253	0.73 (0.54–0.99)
10–14 times	46	115	0.93 (0.63–1.37)
15 times	46	128	0.71 (0.48–1.05)
p for trend			0.10
Height at 9–10 years of age compared to peers			
Much shorter	37	122	0.76 (0.51–1.13)

Variables	Cases N=699	Controls N=1802	OR (95%CI) ^I
Somewhat shorter	121	331	0.88 (0.68–1.12)
About the same	386	902	1.00 (ref)
Somewhat taller	113	331	0.83 (0.64–1.07)
Much taller	41	113	0.91 (0.62–1.34)
Height at 12–13 years of age compared to peers			
Much shorter	34	107	0.82 (0.54–1.24)
Somewhat shorter	134	378	0.83 (0.66–1.05)
About the same	396	914	1.00 (ref)
Somewhat taller	101	309	0.85 (0.66–1.10)
Much taller	33	93	0.88 (0.57–1.34)
Height at 15–16 years of age compared to peers			
Much shorter	40	128	0.74 (0.50–1.10)
Somewhat shorter	154	401	0.92 (0.73–1.15)
About the same	393	941	1.00 (ref)
Somewhat taller	88	251	0.89 (0.67–1.17)
Much taller	23	80	0.70 (0.43–1.14)
Height change over adolescent years			
Remained much shorter	21	67	0.74 (0.46–1.25)
Remained somewhat shorter	70	193	0.86 (0.62–1.17)
Remained about the same as peers	284	648	1.00 (ref)
Remained somewhat taller	43	144	0.74 (0.51–1.08)
Remained much taller	18	47	0.92 (0.52–1.63)
Height at age 18, cm			
Q1:<160	184	435	1.00 (ref)
Q2:160–<165	193	555	0.87 (0.68–1.11)
Q3:165–<170	195	441	1.10 (0.86–1.42)
Q4: 170	127	370	0.89 (0.68–1.17)
p for trend			0.92
Tallest height in adulthood, cm			
Q1:<160	171	415	1.00 (ref)
Q2:160–<165	196	540	0.95 (0.74–1.21)
Q3:165–<170	199	459	1.11 (0.86–1.43)
Q4: 170	133	387	0.93 (0.70–1.22)
p for trend			0.98
Height at reference date, cm			
Q1:<160	213	516	1.00 (ref)
Q2:160–<162.5	96	256	1.01 (0.76–1.36)
Q3:162.5–<167	210	494	1.16 (0.92–1.47)

Variables	Cases N=699	Controls N=1802	OR (95%CI) ¹
Q4: 167	180	535	0.94 (0.73–1.20)
p for trend			0.89
Height change between age 18 and reference date, cm			
–5	85	168	1.12 (0.82–1.54)
>–5<0	158	351	1.12 (0.88–1.41)
No change	422	1154	1.00 (ref)
<0<5	21	90	0.67 (0.40–1.11)
5	13	38	1.09 (0.57–2.09)

¹ Logistic regression models adjusted for age, race, number of pregnancies, use of oral contraceptives, and family history of breast or ovarian cancer

² the most recent time period of BMI assessment refers to BMI at 18 years of age for those younger than 30, BMI at 30 years of age for those younger than 50, and BMI at 50 years of age for those 50 years of age or older at the time of ovarian cancer diagnosis

Table 3

Association between weight change, height and height change and overall and progression-free survival among ovarian cancer cases, HOPE study.

Variables	Status		HR (95%CI) ¹	Progression		HR (95%CI) ¹
	Died N=417	Alive N=282		Yes N=507	No N=192	
Weight change between ages 18 to 30, pounds						
-10	33	22	1.10 (0.75-1.60)	40	15	1.27 (0.90-1.80)
Within 10	139	94	1.00 (ref)	176	57	1.00 (ref)
10- 20	140	103	1.20 (0.94-1.52)	170	73	1.24 (1.00-1.54)
>20	101	58	1.36 (1.05-1.76)	117	42	1.31 (1.04-1.66)
Weight change between ages 30 to 50, pounds						
-10	16	10	1.01 (0.59-1.71)	19	7	0.86 (0.53-1.39)
Within 10	106	56	1.00 (ref)	128	34	1.00 (ref)
10- 20	98	61	0.90 (0.68-1.18)	120	39	0.96 (0.74-1.23)
>20	127	75	1.00 (0.77-1.30)	151	51	1.02 (0.80-1.29)
Weight change between the most recent time period to the reference date, pounds ²						
-10	47	18	1.26 (0.91-1.76)	54	11	1.16 (0.85-1.57)
Within 10	142	122	1.00 (ref)	185	79	1.00 (ref)
10- 20	106	63	1.20 (0.93-1.55)	127	42	1.09 (0.87-1.37)
>20	121	77	1.25 (0.98-1.60)	140	58	1.09 (0.88-1.36)
BMI change over time						
Remained normal weight	130	103	1.00 (ref)	164	69	1.00 (ref)
Increased from underweight/normal to overweight/obese and remained overweight/obese	154	88	1.14 (0.90-1.44)	182	60	1.16 (0.94-1.43)
Remained obese	34	22	1.10 (0.75-1.62)	39	17	1.07 (0.75-1.52)
Decreased from obese to normal	6	5	1.13 (0.49-2.56)	7	4	0.89 (0.42-1.91)
Body parts where gained weight accumulates						
Around the waist and abdomen	219	135	1.00 (ref)	262	92	1.00 (ref)
Around the chest and shoulders	11	4	1.02 (0.55-1.87)	13	2	1.30 (0.74-2.27)
Around the hips and thighs	91	59	0.96 (0.75-1.23)	113	37	1.13 (0.91-1.42)
Equally all over	70	50	0.85 (0.65-1.11)	82	38	0.83 (0.65-1.07)

Variables		Status		HR (95%CI) ^I	Progression		HR (95%CI) ^I
		Died N=417	Alive N=282		Yes N=507	No N=192	
Other areas		26	34	0.67 (0.45–1.02)	37	23	0.80 (0.56–1.13)
Times lost 10 pounds or more and gained them back							
Never		134	76	1.00 (ref)	165	45	1.00 (ref)
1–4 times		182	130	0.90 (0.72–1.13)	219	93	0.83 (0.68–1.02)
5–9 times		48	37	0.87 (0.62–1.21)	60	25	0.86 (0.64–1.16)
10–14 times		23	23	0.63 (0.40–0.99)	30	16	0.61 (0.41–0.91)
15 times		30	16	0.99 (0.66–1.48)	33	13	0.84 (0.58–1.23)
p for trend				0.25			0.06
Height at 9–10 years of age compared to peers							
Much shorter		17	20	0.96 (0.59–1.59)	275	111	1.12 (0.73–1.70)
Somewhat shorter		73	48	1.02 (0.78–1.33)	24	13	1.04 (0.82–1.31)
About the same		224	162	1.00 (ref)	91	30	1.00 (ref)
Somewhat taller		75	38	1.02 (0.78–1.32)	83	30	0.88 (0.69–1.13)
Much taller		27	14	1.42 (0.94–2.12)	33	8	1.58 (1.09–2.29)
Height at 12–13 years of age compared to peers							
Much shorter		16	18	1.14 (0.68–1.90)	21	13	1.27 (0.81–1.98)
Somewhat shorter		73	61	0.79 (0.61–1.03)	98	36	0.83 (0.66–1.05)
About the same		238	158	1.00 (ref)	284	112	1.00 (ref)
Somewhat taller		67	34	1.06 (0.80–1.39)	77	24	0.90 (0.70–1.16)
Much taller		22	11	1.36 (0.88–2.12)	26	7	1.48 (0.98–2.22)
Height at 15–16 years of age compared to peers							
Much shorter		21	19	1.20 (0.76–1.88)	27	13	1.19 (0.80–1.760)
Somewhat shorter		89	65	1.00 (0.78–1.28)	112	42	1.04 (0.84–1.30)
About the same		227	166	1.00 (ref)	278	115	1.00 (ref)
Somewhat taller		60	28	1.26 (0.95–1.68)	68	20	1.18 (0.91–1.54)
Much taller		19	4	2.19 (1.37–3.52)	21	2	2.28 (1.45–3.58)
Height change over adolescent years							

Variables		Status		HR (95%CI) ^I	Progression		HR (95%CI) ^I
		Died N=417	Alive N=282		Yes N=507	No N=192	
Remained much shorter		12	9	1.37 (0.76–2.48)	15	6	1.33 (0.79–2.26)
Remained somewhat shorter		42	28	1.00 (0.71–1.41)	54	16	1.04 (0.77–1.41)
Remained about the same as peers		165	119	1.00 (ref)	200	84	1.00 (ref)
Remained somewhat taller		31	12	1.01 (0.69–1.49)	32	11	0.88 (0.60–1.28)
Remained much taller		14	4	1.65 (0.95–2.86)	16	2	1.82 (1.08–3.05)
Height at age 18, cm							
Q1:<160		108	76	1.00 (ref)	139	45	1.00 (ref)
Q2:160–<165		107	86	0.97 (0.74–1.27)	135	58	0.99 (0.78–1.25)
Q3:165–170		110	85	1.13 (0.86–1.47)	132	63	0.97 (0.76–1.24)
Q4: 170		92	35	1.36 (1.03–1.80)	101	26	1.15 (0.89–1.49)
p for trend				0.02			0.40
Tallest height in adulthood, cm							
Q1:<160		97	74	1.00 (ref)	127	44	1.00 (ref)
Q2:160–<165		113	83	1.03 (0.79–1.36)	140	56	1.01 (0.79–1.28)
Q3:165–170		113	86	1.16 (0.88–1.53)	137	62	1.00 (0.79–1.28)
Q4: 170		94	39	1.39 (1.04–1.85)	103	30	1.13 (0.87–1.47)
p for trend				0.02			0.42
Height at reference date, cm							
Q1:<160		125	88	1.00 (ref)	160	53	1.00 (ref)
Q2:160–<162.5		57	39	0.96 (0.70–1.32)	70	26	0.89 (0.67–1.18)
Q3:162.5–<167		108	102	1.02 (0.78–1.32)	138	72	0.98 (0.78–1.24)
Q4: 167		127	53	1.51 (1.17–1.94)	139	41	1.26 (0.99–1.59)
p for trend				0.003			0.08
Height change between age 18 and reference date, cm							
–5		55	30	0.77 (0.56–1.06)	68	17	0.84 (0.62–1.12)
>–5<0		97	61	0.82 (0.64–1.06)	118	40	0.85 (0.67–1.06)
No change		243	179	1.00 (ref)	294	128	1.00 (ref)
<0<–5		12	9	0.89 (0.50–1.60)	16	5	1.06 (0.64–1.75)

Variables	Status		HR (95%CI) ¹	Progression		HR (95%CI) ¹
	Died N=417	Alive N=282		Yes N=507	No N=192	
5	10	3	1.08 (0.57–2.04)	11	2	1.08 (0.59–1.98)

¹ Cox proportional hazards model adjusted for age at diagnosis (continuous) and FIGO stage

² the most recent time period of BMI assessment refers to BMI at 18 years of age for those younger than 30, BMI at 30 years of age for those younger than 50, and BMI at 50 years of age for those 50 years of age or older at the time of ovarian cancer diagnosis