HHS Public Access

Author manuscript

Ann Surg Oncol. Author manuscript; available in PMC 2020 September 29.

Published in final edited form as:

Ann Surg Oncol. 2016 September ; 23(9): 2988–2997. doi:10.1245/s10434-016-5237-9.

Weight Change Pattern and Survival Outcome of Women with Endometrial Cancer

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Abstract

Objective—The aim of this study was to determine the association between weight change patterns and survival outcomes of women with endometrial cancer.

Methods—This retrospective study examined surgically-staged endometrial cancer cases with available weight information between 1999 and 2013 ($n = 665$). Proportional body mass index (delta-BMI) change at 6 months, 1 and 2 years after hysterectomy was compared with baseline BMI and correlated to patient demographics, tumor characteristics, treatment type, and disease-free survival (DFS) and overall survival (OS).

Results—Mean BMI was 35.6, and 69 % of cases were obese. At 6 months, 1 and 2 years after surgery, 39.1, 51.6, and 57.0 % of the study population, respectively, gained weight compared with pre-treatment baseline. In univariate analysis, 6-month delta-BMI change was significantly associated with DFS and OS, demonstrating bidirectional effects (both $p < 0.001$): 5-year rates, ≥15.0 % delta-BMI loss (33.5 and 59.1 %), 7.5–14.9 % loss (67.3 and 70.0 %), <7.5 % loss (87.8 and 95.7 %), <7.5 % gain (87.2 and 90.3 %), 7.5–14.9 % gain (64.6 and 67.6 %), and ≥15.0 % gain (32.5 and 66.7 %). In multivariable analysis controlling for age, ethnicity, baseline BMI, histology, grade, stage, chemotherapy, and radiotherapy, 6-month delta-BMI change remained an independent prognostic factor for DFS and OS (all $p < 0.05$): adjusted hazard ratios, ≥15 % delta-BMI loss (3.35 and 5.39), 7.5–14.9 % loss (2.35 and 4.19), 7.5–14.9 % gain (2.58 and 3.33), and ≥15.0 % gain (2.50 and 3.45) compared with <7.5 % loss. Similar findings were observed at a 1-year time point ($p < 0.05$). Baseline BMI was not associated with survival outcome ($p > 0.05$).

Conclusion—Our results demonstrated that endometrial cancer patients continued to gain weight after hysterectomy, and post-treatment weight change had bidirectional effects on survival outcome.

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DISCLOSURE The authors did not report any potential conflicts of interest in the study.

Electronic supplementary material The online version of this article (doi:10.1245/s10434–016-5237–9) contains supplementary material, which is available to authorized users.

Endometrial cancer continues to be the most common gynecologic malignancy in the US.[1] While obesity is a well-recognized risk factor for developing endometrial cancer,[2] prognostic implications of body habitus in endometrial cancer seems contradictory. Some studies have shown that increased body habitus is associated with increased endometrial cancer mortality; however, these studies were in a predominantly non-obese population (proportion of obesity, 32–40 %) and may therefore not represent a typical endometrial cancer population.[3–5] Other studies in predominantly obese populations (proportion of obesity, 54–68 %) have concluded that obesity is not associated with survival outcome of endometrial cancer.[6,7] Their findings are based on the rationale that the majority of endometrial cancer is estrogen-dependent disease related to excess adiposity that is associated with low-grade and early-stage disease and a better prognosis.[8] Taken together, identifying how body habitus affects disease prognosis is an important consideration in the management of women with endometrial cancer.

Recently, post-treatment weight change patterns have been reported to have a prognostic effect on survival in certain types of cancer. For instance, post-treatment weight gain is associated with an increased risk of recurrence in breast cancer, while weight change patterns were not associated with survival outcomes in patients with colon cancer.[9,10] Additionally, considerable weight loss is regarded as a poor survival indicator of cancer patients in general.[11] To date, little is known about the association of post-treatment weight change patterns and endometrial cancer prognosis. The objective of this study was to examine the association between weight change patterns and survival outcomes of women with endometrial cancer.

PATIENTS AND METHODS

After Institutional Review Board approval was obtained, cases were identified by utilizing the divisional database for endometrial cancer. Eligibility criteria were consecutive cases of surgically-staged endometrial cancer diagnosed and managed at the Los Angeles County Medical Center between 1999 and 2013, with available weight information during follow-up care. Sarcoma, endometrial hyperplasia, metastatic cancer to the endometrium, and non-hysterectomy cases were excluded from the study. Among the eligible cases, patient demographics, tumor characteristics, postoperative treatment patterns, weight information, and survival outcomes were obtained from medical records. The STROBE guideline was consulted for observational study. Parts of the study population were within the context of our prior studies[6,12–14] Collected patient demographics included patient age, ethnicity, and medical comorbidities, while tumor characteristics included histologic subtype, grade, and stage. Tumor grade was defined as per the International Federation of Gynecology and Obstetrics (FIGO) criteria, and cancer stage was re-classified based on the 2009 FIGO system.[15] Postoperative treatments included systemic chemotherapy and radiotherapy.

Weight information included baseline body mass index [BMI; calculated as weight (kg)/(height (m)^2)] at the time of surgical staging, and BMI at the additional three time points after surgical staging (6 months, 1 and 2 years). This time period was chosen because the majority of endometrial cancer recurrences occur within the first 2 years after treatment.[16] Then, a half faction (1 year) and a quarter fraction (6 months) of the 2-year time window

were set for interval weight change assessment. The usual practice during this time included routine post-treatment surveillance visits scheduled every 3–6 months in the first 2 years, followed by every 6 months up to 5 years after surgery, and then followed by annual visits until 10 years after surgery.[17] BMI was classified as <30, 30–39.9, or ≥40 kg/m^2 per the World Health Organization (WHO) definition.[18] Survival outcomes included disease-free survival (DFS) and overall survival (OS). DFS was defined as the time interval between the date of endometrial cancer surgery and the date of the first recurrence or the last follow-up date if there was no recurrence, and OS was defined as the time interval between the date of endometrial cancer surgery and the date of death due to endometrial cancer or the last follow-up date if the patient is alive.

Delta-BMI change was defined as the interval BMI change between the two time points (expressed as a percentage of the starting BMI). For example, if the patient's BMI at the surgical staging of endometrial cancer and 6 months after surgery was 40 and 42, the 6-month delta-BMI change was calculated as 100 × (42–40)/40 = 5 %. In this study, delta-BMI change was defined as minimum-mild (<7.5 % loss or gain), moderate (7.5–14.9 % loss or gain), and excess (≥15.0 % loss or gain) (see electronic supplementary Method S1).

The primary analysis was to examine the pattern of weight change after endometrial cancer surgery (6 months, 1 and 2 years), and the secondary analysis was to examine the association between the interval weight change pattern and survival outcome (DFS and OS). Continuous variables were assessed for normality using the Kolmogorov–Smirnov test, expressed as mean (standard deviation) or median (range). Statistical significance of continuous variables in multiple groups was examined with a one-way analysis of variance (ANOVA) test. Categorical or ordinal variables were assessed using the χ^2 test. Survival analysis was performed using the log-rank test for univariate analysis and a Cox's proportional hazard regression model for multivariate analysis, expressed with hazard ratio (HR) and 95 % confidence interval (CI). Covariates entered in the final model were the variables with a cutoff value being $p < 0.10$ in univariate analysis. The Kaplan–Meier method was used to construct survival curves. A p value < 0.05 was considered statistically significant (two-tailed), and the Statistical Package of the Social Science (SPSS) version 12.0 (SPSS Inc., Chicago, IL, USA) was used for the analysis.

RESULTS

Overall, 841 women were diagnosed with endometrial cancer during the study period. Of these, 70 (8.3 %) women did not undergo hysterectomy-based surgical staging. Among 771 women who underwent hysterectomy-based surgical staging, 7 (0.9 %) women were excluded because of a lack of baseline BMI data. Of the remaining 764 women, records were examined for the availability of postoperative BMI results at 6-month, 1-year, and 2-year time points; 99 (13.0 %) were excluded due to the lack of the information for any of the three postoperative time points. Collectively, 665 women with endometrial cancer who underwent hysterectomy-based surgical staging with available postoperative BMI information in at least one of three time points represented the study population ($n = 585$ for the 6-month time point, $n = 594$ for the 1-year time point, and $n = 375$ for the 2-year time point).

Patient demographics are shown in Table 1. The mean age was 52.5 years, and the majority of the study population was Hispanic or Latina (70.8 %). Mean baseline BMI was 35.6 kg/m^2, and the majority of patients were obese (69.0 %). Medical comorbidities were prevalent, with hypertension being the most common (55.3 %). The majority of endometrial cancers were endometrioid histology (82.9 %), grade 1 tumor (53.1 %), and stage I disease (70.2 %). Approximately one-quarter of patients received postoperative chemotherapy (26.5 %). Postoperative radiotherapy was administered to nearly one-third of the patients (34.5 %), with whole pelvic radiotherapy (WPRT) being the most common modality (22.1 %). The median follow-up time was 36.4 months (range 6.0–163.3) for the entire cohort; there were 94 (14.1 %) recurrences, with the median time-to-recurrence being 14.2 months; and there were 59 (8.9 %) deaths due to endometrial cancer, with the median time to death being 28.4 months.

Weight change patterns during the postoperative course were examined. During the postoperative follow-up, the proportions of any class of obesity were 69.0, 67.1, 71.6, and 72.3 % at baseline, 6-month, 1-year, and 2-year time points, respectively. At the 6-month time point, 39.1 % of patients gained weight after surgery, with the median delta-BMI change being 2.4 %, and the remaining 60.1 % of patients lost weight, with the median delta-BMI change being −3.4 %. At the 1-year time point, 51.6 % of patients gained weight compared with pre-treatment weight (median delta-BMI change 4.3 %), and the remaining 48.4 % of patients lost weight (−3.0 %). At the 2-year time point, the proportion of patients who gained weight compared with pre-hysterectomy weight was increased to 57.1 % (median delta-BMI changes, 4.6 %), and the remaining 42.9 % of patients lost weight (−3.5 %). Across the three observed time points, there were 330 patients who were available for weight information at all time points (electronic supplementary Fig. S1). The most common weight change pattern was sustained BMI above the baseline level throughout the 2-year follow-up after surgery (30.6 %), and this group had a significantly increasing proportion of obesity over time (baseline, 6-month, 1-year, and 2-year time points: 55.4, 68.3, 73.3, and 74.3 %; $p = 0.016$). There were groups of patients with rebound weight gain after a period of postoperative weight loss (26.7 %).

Correlations between 6-month weight change patterns and clinicopathological factors were examined (Table 2). Delta-BMI change was associated with age, ethnicity, baseline BMI, hypertension, histologic subtype, grade, stage, and adjuvant chemotherapy and radiotherapy (all $p < 0.05$). The majority of significant variables showed a bidirectional association to delta-BMI change. That is, excess (≥15 % loss or gain) and moderate (7.5–14.9 % loss or gain) delta-BMI changes were associated with older age ($p = 0.034$), and non-endometrioid histology ($p = 0.035$), higher grade ($p = 0.001$), higher stage ($p < 0.001$), and greater prevalence of postoperative radiotherapy ($p = 0.038$) and chemotherapy ($p = 0.001$) compared with minimum–mild delta-BMI change (<7.5 % loss or gain). An inverse correlation was seen between delta-BMI change and baseline BMI ($p < 0.001$). Similar results were seen in the correlation between 1-year delta-BMI change and age, baseline BMI, stage, and postoperative chemotherapy (all $p < 0.05$) (electronic supplementary Table S1). Antiglycemic agent was not associated with delta-BMI change in diabetic patients (electronic supplementary Table S2).

Survival analysis for 6-month delta-BMI change was performed. In univariate analysis, 6-month delta-BMI change was significantly associated with 5-year DFS rates, demonstrating a bidirectional association (33.5 % for excess delta-BMI loss, 67.3 % for 7.5–14.9 loss, 87.8 % for <7.5 % loss, 87.2 % for <7.5 % gain, 64.6 % for 7.5–14.9 % gain, and 32.5 % for ≥15 % gain; $p < 0.001$) (Fig. 1a). After controlling for age, ethnicity, baseline BMI, histologic subtype, grade, stage, postoperative radiotherapy and chemotherapy, excess and moderate 6-month delta-BMI changes remained independent prognostic factors for decreased DFS compared with <7.5 % loss (adjusted HRs, 3.35 for ≥15 % delta-BMI loss, 2.35 for 7.5–14.9 % loss, 2.58 for 7.5–14.9 % gain, and 2.50 for ≥ C15 % gain; all $p < 0.05$) (Table 3). Other independent prognostic factors for decreased DFS included age ≥50 years (adjusted HR 1.86; $p = 0.037$), grade 3 tumor (adjusted HR 2.44; $p = 0.006$), and stage III–IV disease (adjusted HR 5.51; $p < 0.001$). Additionally, 6-month delta-BMI change was significantly associated with 5-year OS rates (59.1, 70.0, 95.7, 90.3, 67.6, and 66.7 %; $p < 0.001$) (Fig. 1b). On multivariate analysis, excess and moderate 6-month delta-BMI changes remained an independent prognostic factor for decreased OS compared with <7.5 % loss (adjusted HRs, 5.39 for ≥15 % delta-BMI loss, 4.19 for 7.5–14.9 % loss, 3.33 for 7.5–14.9 % gain, and 3.45 for 7.5–14.9 % gain; all $p < 0.05$) (Table 4). Baseline BMI was not associated with DFS and OS (both $p > 0.05$). A bidirectional association was re-demonstrated between moderate–excess 1-year delta-BMI changes and decreased DFS ($p < 0.001$) (Fig. 1c). On multivariate analysis, excess 1-year delta-BMI change remained an independent prognostic factor associated with decreased DFS (adjusted HR, 3.47 for ≥15 % loss, and 3.05 for ≥15 % gain; both $p < 0.05$) (electronic supplementary Table S4). Moderate-excess 1-year delta-BMI loss remained as an independent prognostic factor for decreased OS on multivariate analysis (adjusted HR 3.03 for ≥15 % loss, and 4.67 for 7.5–14.9 % loss; both $p < 0.05$) (Fig. 1d and electronic supplementary Table S4).

DISCUSSION

The key findings of this study are that endometrial cancer patients continued to gain weight after surgical staging and that both weight loss and gain patterns were significantly associated with survival outcome of endometrial cancer. A parabolic relationship was demonstrated between the interval weight change and the risk of cancer recurrence/mortality. Interestingly, the magnitudes of significance for survival outcome were similar between weight loss and gain, endorsing the importance of monitoring weight changes during postoperative surveillance follow-up.

Several hypotheses can be proposed for the causality between weight gain and an increased risk of cancer recurrence and mortality. Of these, the most commonly described etiology may be the unopposed estrogen theory from excess adipose tissue. Enhanced conversion of androgen to estradiol in adipose tissue has been described to result in a constant mitogenic stimulation that can potentially trigger tumor progression.[2] Hyperinsulinemia related to obesity may be another etiology as it promotes insulin-like growth factor secretion (IGF-1) which can activate mitogenic and pro-angiogenic pathways while inhibiting apoptosis.[19] A role of inflammation is also an important consideration. Obesity is a state of chronic inflammation that can trigger mitogenic effects, including tumor promoter release from inflammatory cells. These cells can also generate reactive oxygen species.[20] Furthermore,

pro-inflammatory cytokines secreted by adipocytes have been implicated in tumor cell growth and progression.[21]

The role of adipocytes in the tumor microenvironment deserves special attention. It has been suggested that adipocytes can be reprogrammed to cancer-associated adipocytes, which promote adhesion, migration, and invasion of tumor cells, as well as releasing fatty acids that are used by cancer cells as a source of energy.[20,21] In addition, nutritional excess is a main inducer of cellular stress that can lead to the activation of endoplasmic reticulum stress in visceral adipocytes. This has been significantly related to aggressive tumor behavior resulting in poor survival outcome of endometrial cancer.[22]

An important factor for weight gain and decreased survival outcome in cancer patients is possible suboptimal chemotherapy or radiotherapy in obese patients. A recent meta-analysis reported that up to 40 % of obese patients receive limited and reduced doses of chemotherapy when not based on actual body weight, and this has been suggested to be the main contributing factor related to poor survival outcome of obese patients in gynecologic cancer.[23] A similar concept applies to the suboptimal efficacy of radiotherapy in the obese population, and obesity is known to be a prognostic factor for increased risk of recurrence after WPRT for pelvic cancer.[24,25] Therefore, it is paramount that chemotherapy doses are calculated by actual body weight.[23]

Other possible associations linking weight gain and poor outcome of endometrial cancer include low levels of physical activity and low socioeconomic status. Reduced physical activity and sedentary lifestyle are related to obesity, and it is suggested that even light exercise and moderate physical activity were associated with improved OS in endometrial cancer patients.[2,26] Low socioeconomic status is reported as an independent predictor for poor cancer treatment adherence, resulting in decreased survival outcome.[27] Because low socioeconomic status is associated with an increased risk of obesity,[28] this association may be an explanation for weight gain and decreased survival in endometrial cancer.

In the present study, moderate/excess weight loss was associated with poor survival in endometrial cancer patients. Similar to this project’s findings, several other studies have suggested that any weight loss after cancer diagnosis was associated with lower response to chemotherapy, increased toxicity, and reduced survival rates.[11,29] There are several possible explanations for this link. First, weight loss may lead to a significant impairment of the immune system, particularly deficits in cell-mediated immunity, which can result in tumor progression.[30] Second, reduction in body mass may increase toxicity to adjuvant therapy and result in decreased survival outcome.[31] Finally, cachexia syndrome is characterized by a systemic inflammatory response, anorexia, and weight loss.[32] This may result in impaired immune function, propensity for infections, tolerance to anticancer treatments, and psychosocial distress.[32]

CONCLUSIONS

Awareness of the potential significance of post-treatment weight change patterns on survival outcome of women with endometrial cancer needs to be considered in practice. Routine and

accurate monitoring of weight change, patient education and counseling based on weight change patterns, as well as proper referrals for diet and exercise programs, are suggested as an integral part of a multidisciplinary approach in the management of endometrial cancer patients. Further investigation into postoperative weight changes in the endometrial cancer patient population and patient outcomes is warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

FUNDING Ensign Endowment for Gynecologic Cancer Research (to Koji Matsuo).

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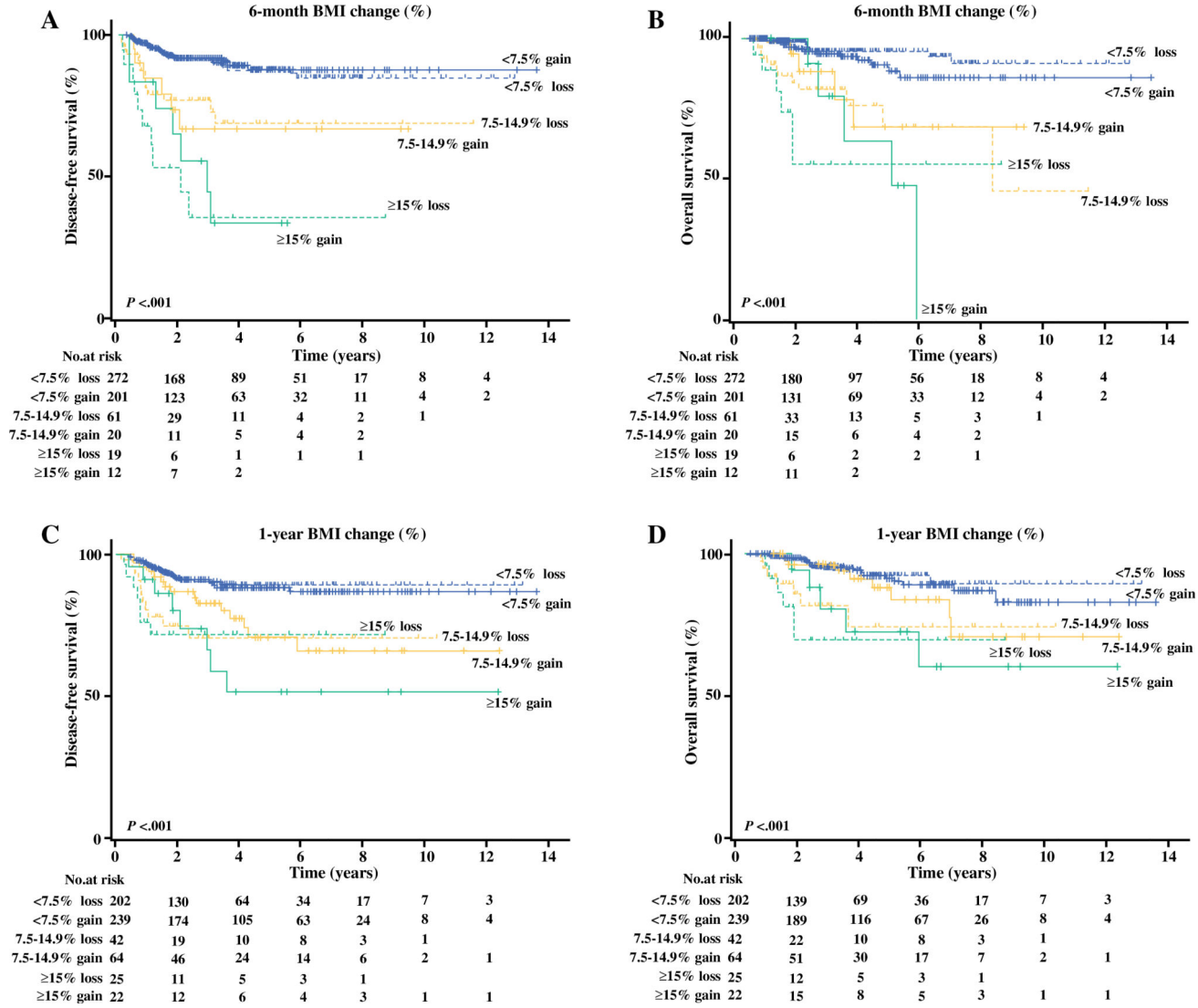

FIG. 1.

Survival curves based on 6-month delta-BMI change for **a** disease-free survival and **b** overall survival; and 1-year delta-BMI change for **c** disease-free survival and **d** overall survival. Log-rank test for *p* values. *BMI* body mass index

TABLE 1

Patient demographics

	***N* = 665**
Age (years)	52.5 (±10.1)
<50	237 (35.6)
≥50	428 (64.4)
Ethnicity	
Caucasian	68 (10.2)
African	28 (4.2)
Hispanic	471 (70.8)
Asian	98 (14.7)
BMI (kg/m^2)	35.6 (±9.6)
<30	206 (31.0)
30–39.9	273 (41.1)
≥40	186 (28.0)
Hypertension	
No	297 (44.7)
Yes	368 (55.3)
Diabetes mellitus	
No	453 (68.1)
Yes	212 (31.9)
Hypercholesterolemia	
No	500 (75.2)
Yes	165 (24.8)
Histologic subtype	
Endometrioid	551 (82.9)
Serous	33 (5.0)
Clear cell	13 (2.0)
Mixed	63 (9.5)
Others	5 (0.8)
Grade	
1	353 (53.1)
2	164 (24.7)
3	148 (22.3)
Stage	
I	467 (70.2)
II	54 (8.1)
III	99 (14.9)
IV	45 (6.8)
Postoperative chemotherapy	
None	489 (73.5)
Carboplatin + paclitaxel	161 (24.2)

	***N* = 665**
Other	15 (2.3)
Postoperative radiotherapy	
None	435 (65.4)
ICBT alone	83 (12.5)
WPRT ± ICBT	147 (22.1)

Data are expressed as mean (±SD) or *n* (%)

111 (16.7 %) cases received both chemotherapy and radiotherapy

BMI body mass index, *ICBT* intracavitary brachytherapy, *WPRT* whole pelvic radiotherapy, *SD* standard deviation

Ann Surg Oncol. Author manuscript; available in PMC 2020 September 29.

TABLE 2

Correlations between 6-month delta-BMI change and clinicopathological factors

	≥15 % loss [*n* = 19 (2.9 %)]	**7.5–14.9 % loss [*n* = 61 (9.2 %)]**	**<7.5 % loss[a] [*n* = 272 (40.9 %)]**	**<7.5 % gain [*n* = 201 (30.2 %)]**	**7.5–14.9 % gain [*n* = 20 (3.0 %)]**	**≥15 % gain [*n* = 12 (1.8 %)]**	***p* value**
Age (years)	56.5 (±8.7)	50.8 (±9.9)	53.2 (±10.1)	51.0 (±10.3)	54.3 (±10.3)	55.9 (±11.1)	**0.034**
<50	3 (15.8)	27 (44.3)	89 (32.7)	82 (40.8)	5 (25)	4 (33.3)	
≥50	16 (84.2)	34 (55.7)	183 (67.3)	119 (59.2)	15 (75)	8 (66.7)	
Ethnicity							**0.008**
Caucasian	3 (15.8)	12 (19.7)	28 (10.3)	16 (8.0)	2 (10)	1 (8.3)	
African	2 (10.5)	3 (4.9)	14 (5.1)	4 (2.0)	0	3 (25.0)	
Hispanic	11 (57.9)	37 (60.7)	192 (70.6)	152 (75.6)	16 (80)	4 (33.3)	
Asian	3 (15.8)	9 (14.8)	38 (14.0)	29 (14.4)	2 (10)	4 (33.3)	
Pre-treatment BMI	36.6 (±10.3)	40.1 (±12.8)	36.1 (±9.1)	34.7 (±9.1)	30.9 (±5.9)	26.0 (±5.3)	**<0.001**
<30	5 (26.3)	14 (23.0)	74 (27.2)	70 (34.8)	10 (50)	11 (91.7)	
30–39.9	9 (47.4)	19 (31.1)	116 (42.6)	80 (39.8)	9 (45)	1 (8.3)	
≥40	5 (26.3)	28 (45.9)	82 (30.1)	51 (25.4)	1 (5)	0	
Hypertension							**0.026**
No	6 (31.6)	32 (52.5)	112 (41.2)	99 (49.3)	9 (45)	10 (83.3)	
Yes	13 (68.4)	29 (47.5)	160 (58.8)	102 (50.7)	11 (55)	2 (16.7)	
Diabetes mellitus							0.11
No	12 (63.2)	42 (68.9)	170 (62.5)	146 (72.6)	13 (65)	11 (91.7)	
Yes	7 (36.8)	19 (31.1)	102 (37.5)	55 (27.4)	7 (35)	1 (8.3)	
Hypercholesterolemia							0.53
No	15 (78.9)	50 (82.0)	204 (75)	150 (74.6)	17 (85)	11 (91.7)	
Yes	4 (21.1)	11 (18.0)	68 (25)	51 (25.4)	3 (15)	1 (8.3)	
Histologic subtype							**0.035**
Endometrioid	13 (68.4)	49 (80.3)	223 (82.0)	176 (87.6)	16 (80)	6 (50)	
Serous	2 (10.5)	4 (6.6)	12 (4.4)	9 (4.5)	2 (10)	2 (16.7)	
Clear cell	1 (5.3)	1 (1.6)	4 (1.5)	4 (2.0)	2(10)	0	
Mixed	3 (15.8)	7(11.5)	30 (11.0)	10 (5.0)	0	4 (33.3)	
Others	0	0	3 (1.1)	2 (1.0)	0	0	
Grade							**0.001**

	≥15 % loss [*n* = 19 (2.9 %)]	7.5–14.9 % loss [*n* = 61 (9.2 %)]	<7.5 % loss[a] [*n* = 272 (40.9 %)]	<7.5 % gain [*n* = 201 (30.2 %)]	7.5–14.9 % gain [*n* = 20 (3.0 %)]	≥15 % gain [*n* = 12 (1.8 %)]	*p* value
1	4 (21.1)	29 (47.5)	148 (54.4)	125 (62.2)	9 (45)	2 (16.7)	
2	5 (26.3)	12 (19.7)	68 (25)	45 (22.4)	5 (25)	5 (41.7)	
3	10 (52.6)	20 (32.8)	56 (20.6)	31 (15.4)	6 (30)	5 (41.7)	
Stage							**<0.001**
I	7 (36.8)	36 (59.0)	204 (75.0)	158 (78.6)	10 (50)	2 (16.7)	
II	0	7 (11.5)	19 (7.0)	15 (7.5)	2 (10)	1 (8.3)	
III	7 (36.8)	13 (21.3)	34 (12.5)	19 (9.5)	3 (15)	4 (33.3)	
IV	5 (26.3)	5 (8.2)	15 (5.5)	9 (4.5)	5 (20)	5 (41.7)	
Postoperative radiotherapy							**0.038**
None	11 (57.9)	35 (57.4)	175 (64.3)	146 (72.6)	13 (65)	5 (41.7)	
ICBT alone	1 (5.3)	6 (9.8)	45 (16.5)	23 (11.4)	2 (10)	3 (25)	
WPRT ± ICBT	7 (36.8)	20 (32.8)	52 (19.1)	32 (15.9)	5 (25)	4 (33.3)	
Postoperative chemotherapy							**<0.001**
None	5 (26.3)	37 (60.7)	211 (77.6)	163 (81.1)	10 (50)	5 (41.7)	
Carboplatin + paclitaxel	12 (63.2)	22 (36.1)	57 (21.0)	32 (15.9)	10 (50)	7 (58.3)	
Other	2 (10.5)	2 (3.3)	4 (1.5)	6 (3.0)	0	0	

Data are expressed as mean (±SD) or *n* (%)

One-way ANOVA or χ^2 test for *p*-values. Significant *p* values are shown in bold

[a]Including cases with no interval BMI change

BMI body mass index, *ICBT* intracavitary brachytherapy, *WPRT* whole pelvic radiotherapy, *ANOVA* analysis of variance, *SD* standard deviation

TABLE 3

Disease-free survival based on 6-month delta-BMI change

	N	5-years (%)	Univariate		Multivariate	
			HR (95 % CI)	*p* value	HR (95 % CI)	*p* value
Age (years)				**0.001**		
<50	237	89.1	1		1	
≥50	428	77.8	2.24 (1.3–3.67)		1.86 (1.04–3.35)	**0.037**
Ethnicity				**<0.001**		
Non-hispanic	194	71.5	1		1	
Hispanic	471	85.8	0.50 (0.33–0.75)		0.65 (0.41–1.04)	0.073
Pre-treatment BMI				**0.034**		
<30	206	77.3	1		1	
≥30	459	84.0	0.64 (0.43–0.97)		1.44 (0.86–2.42)	0.17
Hypertension				0.74		
No	297	82.6	1			
Yes	368	81.4	1.07 (0.71–1.61)			
Diabetes mellitus				0.57		
No	453	81.1	1			
Yes	212	83.5	0.88 (0.57–1.37)			
Hypercholesterolemia				0.87		
No	500	81.3	1			
Yes	165	83.1	1.04 (0.66–1.64)			
Histologic subtype				**<0.001**		
Endometrioid	551	88.4	1		1	
Non-endometrioid	114	50.6	6.46 (4.30–9.68)		1.49 (0.84–2.66)	0.18
Grade				**<0.001**		
1–2	517	89.6	1		1	
3	148	54.5	7.12 (4.70–10.8)		2.44 (1.30–4.59)	**0.006**
Stage				**<0.001**		
I–II	521	92.9	1		1	
III–IV	144	46.0	11.1 (7.07–17.3)		5.51 (2.72–11.2)	**<0.001**

Ann Surg Oncol. Author manuscript; available in PMC 2020 September 29.

	N	5-years (%)	Univariate		Multivariate	
			HR (95 % CI)	*p* value	HR (95 % CI)	*p* value
Postoperative chemotherapy				**<0.001**		
None	489	93.1	1		1	
Yes	176	52.3	9.32 (5.90–14.7)		1.54 (0.76–3.12)	0.23
Postoperative radiotherapy				**<0.001**		
None or ICBT alone	518	86.7	1		1	
WPRT ± ICBT	147	67.1	2.80 (1.86–4.20)		1.04 (0.64–1.69)	0.89
Delta-BMI change				**<0.001**		
<7.5 % loss[a]	272	87.8	1		1	
<7.5 % gain	201	87.3	0.92 (0.50–1.68)		1.22 (0.65–2.27)	0.53
7.5–14.9 % loss	61	67.0	3.08 (1.63–5.82)		2.35 (1.21–4.56)	**0.011**
7.5–14.9 % gain	20	64.6	3.35 (1.38–8.14)		2.58 (1.03–6.45)	**0.043**
≥15 % loss	19	33.5	8.96 (4.30–18.7)		3.35 (1.55–7.25)	**0.002**
≥15 % gain	12	32.5	7.09 (3.07–16.4)		2.50 (1.01–6.19)	**0.048**

Log-rank test for univariate analysis, and a Cox proportional hazard regression model for multivariate analysis. Covariates entered in the final model were the variables with $p < 0.10$ in univariate analysis. Significant *p* values are shown in bold

[a]Including cases with no interval BMI change

BMI body mass index, *5-years (%)* 5-years rate, *HR* hazard ratio, *CI* confidence interval, *ICBT* intracavitary brachytherapy, *WPRT* whole pelvic radiotherapy

TABLE 4

Overall survival based on 6-month delta-BMI change

	N	5-years (%)	Univariate		Multivariate	
			HR (95 % CI)	*p* value	HR (95 % CI)	*p* value
Age (years)				**0.042**		
<50	237	92.7	1		1	
≥50	428	85.9	1.82 (1.01–3.27)		1.15 (0.56–2.37)	0.71
Ethnicity				**0.021**		
Non-hispanic	194	82.2	1		1	
Hispanic	471	90.8	0.55 (0.32–0.92)		0.65 (0.35–1.20)	0.17
Pre-treatment BMI				0.06		
<30	206	84.5	1		1	
≥30	459	90.3	0.62 (0.37–1.03)		1.19 (0.62–2.28)	0.60
Hypertension				0.92		
No	297	88.4	1			
Yes	368	88.4	0.98 (0.58–1.63)			
Diabetes mellitus				0.38		
No	453	88.0	1			
Yes	212	89.3	0.78 (0.44–1.37)			
Hypercholesterolemia				0.61		
No	500	88.4	1			
Yes	165	88.4	0.86 (0.47–1.56)			
Histologic subtype				**<0.001**		
Endometrioid	551	94.1	1		1	
Non-endometrioid	114	62.0	8.86 (5.25–15.0)		2.06 (1.01–4.20)	**0.048**
Grade				**<0.001**		
1–2	517	94.8	1		1	
3	148	65.6	7.88 (4.62–13.4)		2.20 (0.97–5.01)	0.06
Stage				**<0.001**		
I–II	521	95.8	1		1	
III–IV	144	65.8	14.3 (7.56–26.8)		5.56 (2.04–15.1)	**0.001**

	N	5-years (%)	Univariate		Multivariate	
			HR (95 % CI)	*p* value	HR (95 % CI)	*p* value
Postoperative chemotherapy				**<0.001**		
None	489	95.7	1		1	
Yes	176	69.0	10.6 (5.74–19.7)		1.61 (0.66–3.96)	0.30
Postoperative radiotherapy				**<0.001**		
None or ICBT alone	518	91.6	1		1	
WPRT ± ICBT	147	79.4	3.01 (1.80–5.02)		1.13 (0.60–2.14)	0.70
Delta-BMI change				**<0.001**		
<7.5 % loss[a]	272	95.7	1		1	
<7.5 % gain	201	90.3	1.78 (0.78–4.06)		2.02 (0.87–4.70)	0.10
7.5–14.9 % loss	61	70.0	6.72 (2.90–15.6)		4.19 (1.73–10.2)	**0.001**
7.5–14.9 % gain	20	67.6	5.03 (1.58–16.0)		3.33 (1.01–11.1)	**0.049**
≥15 % loss	19	59.1	14.4 (5.22–39.9)		5.39 (1.83–15.9)	**0.002**
≥15 % gain	12	66.7	10.3 (3.50–30.3)		3.50 (1.08–11.3)	**0.036**

Log-rank test for univariate analysis, and a Cox proportional hazard regression model for multivariate analysis. Covariates entered in the final model were the variables with $p < 0.10$ in univariate analysis. Significant *p* values are shown in bold

[a]Including cases with no interval BMI change

BMI body mass index, *5-years (%)* 5-year rate, *HR* hazard ratio, *CI* confidence interval, *ICBT* intracavitary brachytherapy, *WPRT* whole pelvic radiotherapy