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# Endometrial cancer in an increasingly obese population: Exploring alternative options when surgery may not cut it



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ARTICLE INFO	A B S T R A C T
<i>Keywords:</i> Obesity Endometrial cancer Hormonal therapy Medically inoperable NSQIP	<i>Objectives:</i> The study objectives were to describe outcomes of obese patients with early endometrial cancer following primary non-surgical treatment, assess predictors of response, and estimate the increased surgical risk for these women. <i>Methods:</i> Retrospective chart review identified women with early stage endometrial cancer at a single institution with BMI ≥ 30 kg/m <sup>2</sup> who did not undergo surgery as primary treatment modality due to obesity and medical co-morbidities. Clinicopathologic factors were abstracted, characteristics of responders vs. non-responders compared and the National Surgical Quality Improvement Program (NSQIP) surgical risk calculator utilized to quantify surgical risks. <i>Results:</i> Fifty-one patients were identified, with a mean BMI of 49.0 kg/m <sup>2</sup> . The NSQIP calculator predicted a significantly higher complication rate for our cohort compared to the expected average risk for hysterectomy (18.8% vs 7.2%, <i>p</i> < .0001). The majority of patients were identified between responders and on-responders with regard to NSQIP scores, BMI, co-morbidities or age. Among those with persistent or progressive disease, 87.5% responded to secondary treatment. Only one death was from cancer progression. Two individuals died following treatment complications (one surgical, one chemotherapy); the remaining twelve deaths were due to pre-existing co-morbidities. <i>Conclusions:</i> Hormone and radiation therapy are both viable options for obese patients deemed to have too significant risk of surgical complications. Pursuing surgical intervention in this population may do more harm than good.

# 1. Introduction

Endometrial cancer is the most common gynecologic cancer in the United States (Siegel et al., 2017). Since 2002, rates have increased approximately 2.5% annually, including a 10% increase from 2006 to 2012 (Constantine et al., 2017). Over 61,000 new cases were expected in 2017, with nearly 11,000 expected deaths (Siegel et al., 2017). Excess adiposity is a well-established risk factor for endometrial cancer and the rising obesity epidemic in the United States is likely a large contributor to these recent trends (Reeves et al., 2011). It is estimated that around 70% of adults aged 20 and over are overweight or obese (Ljungvall and Zimmerman, 2012). Furthermore, between 2009 and 2034, the number of people with diabetes is expected to increase from

23.7 million to 44.1 million (Huang et al., 2009). In addition to increasing one's lifetime risk for endometrial cancer, obesity and diabetes predispose patients to a number of other medical co-morbidities and potential surgical complications.

Surgical intervention, including hysterectomy with bilateral salpingo-oophorectomy and possible lymph node evaluation, is the standard treatment for early stage endometrial cancer; however, obesity and associated co-morbidities place these patients at high risk for surgical complications. As such, up to 10% of patients may be deemed medically inoperable due to excessive surgical risk (Niazi et al., 2005; Podzielinski et al., 2012; Acharya et al., 2016). If current trends persist, the number of patients deemed medically inoperable due to obesity will continue to rise as well. As such, exploring alternative treatment

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https://doi.org/10.1016/j.gore.2018.04.009 Received 18 February 2018; Received in revised form 19 April 2018; Accepted 21 April 2018 Available online 24 April 2018 2352-5789/ © 2018 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/BY-NC-ND/4.0/). options for this patient population is crucial, and radiation and hormonal therapy have often been utilized for non-surgical candidates. Several studies have investigated outcomes after radiation therapy alone in early endometrial cancer and it remains a viable option for local disease control in patients who cannot undergo surgery following an endometrial cancer diagnosis (SGO Clinical Practice Endometrial Cancer Working Group et al., 2014; Potish et al., 1985a; Varia et al., 1987a; Shenfield et al., 2009a).

Hormonal therapy may be another treatment alternative for this particular group of patients. Hormonal treatment for endometrial cancer can include aromatase inhibitors, luteinizing hormone-releasing hormone agonists, selective estrogen receptor modulators, or progestins. Aromatase inhibitors and luteinizing hormone-releasing hormone agonists both act by reducing serum levels of circulating estrogen. Selective estrogen receptor modulators work by preventing any circulating estrogen from stimulating further growth of any cancer cells. Progestins are synthetic progestogens that have effects similar to those of progesterone, and are the most commonly used hormonal treatment for endometrial cancer. The histologic effect of progesterone has been validated in a number of studies of serial biopsies obtained from patients in whom surgery or irradiation was contraindicated (Kohorn, 2012; Mentrikoski et al., 2012; Saegusa and Okayasu, 1998; Wheeler et al., 2007). Given the increasing numbers of patients with obesity, understanding outcomes of radiation and hormone therapy in early endometrial cancer as well as potential surgical risks will be of paramount importance for the ability to adequately counsel these patients on treatment options. The study objectives were to describe the outcomes of obese patients with early endometrial cancer following primary non-surgical treatment, to assess predictors of response, and to estimate the increased surgical risk for these women.

## 2. Methods

Prior to study commencement, approval was obtained from the institutional review board (IRB) at the University of Virginia. Retrospective chart review was performed using the Clinical Data Repository and the University of Virginia Tumor Registry and identified women with clinical stage I and II endometrial cancer, with a body mass index (BMI)  $\ge 30 \text{ kg/m}^2$  who did not undergo surgery as primary treatment modality from January 1, 2000 to December 31, 2016. Inclusion criteria included age of at least 18 years of age, early stage endometrial cancer diagnosis with histologic confirmation, primary treatment modality with either chemotherapy, hormonal or radiation therapy, BMI  $\ge 30 \text{ kg/m}^2$  documented at time of diagnosis, at least one year of documented follow-up care after diagnosis at UVA. All histologic subtypes were included. Exclusion criteria included evidence of stage III or IV disease based on clinical evaluation (imaging or biopsy),  $BMI < 30 \text{ kg/m}^2$  at time of diagnosis, surgery as primary treatment modality, decision to omit surgical intervention for fertility-sparing or other reasons not related to obesity or significant co-morbidities, and lack of documented follow-up after initial diagnosis.

Data were abstracted by review of all clinical documentation in the electronic medical records, including those documents sent and scanned in through outside referring physicians. Gynecologic pathologists reviewed all pathology. Data abstracted included age at diagnosis, race, insurance status, BMI at time of diagnosis, obstetric history, comorbidities, clinical stage at diagnosis, grade, histology, initial and subsequent treatment modalities, including response and complications, recurrences, date of death or last follow-up, pathology reports of all excisional procedures (including biopsies or curettage), all imaging reports, all radiotherapy treatments reports and operative reports. Major co-morbidities included in analysis were diabetes, hypertension, coronary artery disease, congestive heart failure, hyperlipidemia, venous thromboembolism, liver disease, chronic kidney disease, asthma and chronic obstructive pulmonary disease (COPD). Of note, asthma and COPD were considered together as a single co-morbidity. Furthermore, co-morbidities other than those listed above, only contributed to individuals' total number of co-morbidities if they were deemed by the authors to be significant.

Patients were followed until death, loss to follow-up, or time of data abstraction in August 2017. Disease status at each follow-up time point was determined by clinical exam, imaging, or endometrial sampling. Status at time of follow-up was characterized as complete response, partial response, stable disease, or progressive disease. Complete response was defined as no clinical evidence of disease on exam or imaging, or benign endometrium without atypia on subsequent endometrial sampling following treatment. Partial response was defined as clinically or radiographically improved exam in the setting of persistent disease, improvement in grade, or diagnosis of atypical hyperplasia following treatment for carcinoma. No response was defined as no change in clinical examination or imaging, or persistence of the initial tissue diagnosis on subsequent tissue sample. Progression was defined as any progressive grade or increasing disease burden following initial treatment. These definitions reflect methods previously reported by others who have examined endometrial response rates to primary hormonal treatment among patients in whom surgery is not an option (Baker et al., 2017; Hubbs et al., 2013). Individuals with complete response or partial response were categorized as having "Response" and individuals with stable or progressive disease were categorized as having "No Response." Time to response was defined as the time of initial biopsy to first negative clinical exam, negative imaging or negative biopsy.

Complications and mortality from surgery were estimated for each patient at the time of initial diagnosis by using the American College of Surgeons National Surgical Quality Improvement Program's (NSQIP) Surgical Risk Calculator. The NSQIP Calculator is a decision-support tool based on reliable multi-institutional clinical data, which can be used to estimate the risks of most operations. For each individual in our cohort, their personal and health history was logged into the Risk Calculator with laparoscopic hysterectomy and bilateral salpingo-oophorectomy as the planned theoretical procedure. Their chance of an unfavorable outcome, including a major complication, any complication, or death, was calculated based on their unique information. These calculated estimates of unfavorable outcomes were then compared to that of age-matched healthy controls. The same was done for open hysterectomy and bilateral salpingo-oophorectomy. Calculations for complete surgical staging were not considered.

Response rates, including stratification of complete response, partial response, stable disease and progressive disease were examined among the primary radiation and hormonal therapy groups. Demographic and clinical characteristics were compared between the primary radiation group and the hormonal therapy group. Demographic and clinical characteristics of responders and non-responders were compared as well. Statistical analysis was performed using IBM SPSS Statistics (version 24.0, Armonk, NY), and student's *t*-test and chi-squared tests were employed as indicated.

# 3. Results

Data abstraction identified 130 patients with endometrial cancer and BMI  $\geq$  30 kg/m<sup>2</sup> who did not receive surgery as primary treatment modality. Forty-nine patients were excluded because of advanced disease. Thirteen patients were excluded for other medical or personal reasons precluding them from immediate planned surgery (five declined offered surgery, three excluded due to recent myocardial infarction (MI) or pulmonary embolism (PE) who required a course of anti-coagulant prior to surgery, one who had planned radiation to shrink primary tumor prior to surgery, two due to severe liver disease, one Jehovah's witness with severe anemia had surgery after optimization and one was delayed for coordination with general surgery for a concomitant procedure). Six patients were excluded because of desire to maintain fertility and 11 excluded due to loss to follow-up shortly

#### Table 1

Clinical and demographic characteristics of obese early stage endometrial cancer patients who did not undergo surgery as primary treatment (n = 51).

Clinical and pathologic characteristics	n (%) or mean (range)
Age (years)	66 (39–88)
Race/ethnicity	
Caucasian	44 (86.3)
African-American	7 (13.7)
BMI (kg/m <sup>2</sup> )	49.0 (30.0-84.4)
BMI range	
$\geq$ 30 and < 40 kg/m <sup>2</sup>	12 (23.5)
$\geq$ 40 and < 50 kg/m <sup>2</sup>	19 (37.3)
$\geq$ 50 and < 60 kg/m <sup>2</sup>	11 (21.6)
$\geq$ 60 kg/m <sup>2</sup>	9 (17.6)
NSQIP scores (predicted)	
Risk of complication with laparoscopy	14.5 (5.3-40)
Risk of mortality with laparoscopy	1.3 (0-22.7)
Risk of complication with laparotomy	18.7 (7.3-46.4)
Risk of mortality with laparotomy	1.6 (0-26.4)
Number of comorbidities	3.25 (0-7)
Presence of specified comorbidity	
Hypertension	40 (78.4)
Diabetes	28 (54.9)
Congestive heart failure	18 (35.3)
Hyperlipidemia	14 (27.5)
Asthma/COPD	9 (17.6)
Chronic kidney disease	9 (17.6)
Coronary artery disease	8 (15.7)
Clinical stage	
IA	38 (74.5)
IB	7 (13.7)
II	6 (11.8)
Grade	
I	43 (84.3)
II	3 (5.9)
III	5 (9.8)
Histology	
Endometrioid	48 (94)
UPSC	1 (2)
Carcinoma, NOS	1 (2)
Mixed	1 (2)
Initial treatment	
Radiation	25 (49.0)
Hormone therapy	23 (45.1)
Combination	3 (5.9)
Chemotherapy	0 (0)

after diagnosis. Treatment plans were developed for the remaining 51 patients. Follow up sufficient to assess response occurred in 46 women (90%), whereas response to treatment could not be assessed in the remaining five women due to loss to follow up immediately after development of treatment plan. Median follow-up time for the cohort of 46 evaluable women was 20.5 months.

Clinical and demographic characteristics of the entire cohort are described in Table 1. Mean age at diagnosis was 66.2 years, the vast majority were White (86%) and the mean BMI was 49.0 kg/m<sup>2</sup>. On average, the patients had just over three major co-morbidities. Hypertension and diabetes mellitus were the most common co-morbidities, present in 78% (n = 40) and 55% (n = 28) of individuals respectively. The majority of patients (n = 38, 74.5%) were stage 1A, followed by stage IB (n = 7, 13.7%) and stage II (n = 6, 11.8%). Endometrioid adenocarcinoma was the most frequent histology seen (n = 48, 94.1%). The majority were also grade 1 (n = 43, 84.3%).

Treatments employed included 45.1% (n = 23) of patients received hormone therapy, 49% (n = 25) received radiation therapy and 5.9% (n = 3) received both concurrently. All individuals who received hormone therapy in addition to radiation were on Megestrol acetate (Megace). Tables 2a and 2b shows the breakdown of initial and subsequent treatment modalities for the group, as well as the best response for each. Of the patients who received hormonal therapy as primary treatment, the levonorgestrel intrauterine device (Mirena) was placed Table 2a

Clinical response to initial treatment
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Treatment modality		Response		No response
Hormonal $(n = 21)$		8 (38.1%)		13 (61.9%)
Radiation ( $n = 22$ )		14 (63.6%)		8 (36.4%)
Combination $(n = 3)$		3 (100%)		(0) 0%
<sup>a</sup> Total group ( $n = 46$ )		25 (54.3%)		21 (45.7%)
	Complete	Partial	Stable	Progression
	Response	Response		-
Hormonal				
Mirena $(n = 15)$	4 (26.7%)	1 (6.7%)	6 (40%)	4 (26.7%)
Megace $(n = 6)$	3 (50%)	0 (0%)	2 (33.3%)	1 (16.7%)
Radiation				
External $(n = 0)$	-	-	-	-
Brachytherapy	7 (70%)	0 (0%)	2 (20%)	1 (10%)
(n = 10)				
Combination	6 (50%)	1 (8.3%)	2 (16.7%)	3 (25%)
(n = 12)				
Combination	2 (66.7%)	1 (33.3%)	0 (0%)	0 (0%)

<sup>a</sup> 46 of the 51 individuals in the cohort were evaluable. Response was not evaluable for n = 2 patient who received Mirena as initial treatment and n = 3 who received Radiation.

#### Table 2b

Clinical response to secondary treatmen	Clinical	response	to	secondary	treatmen
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Treatment modality	Response	No response
Hormonal $(n = 5)$	4 (80%)	1 (20%)
Radiation $(n = 5)$	5 (100%)	0 (0%)
Chemotherapy $(n = 1)$	0 (0%)	1 (100%)
Surgery $(n = 4)$	4 (100%)	0 (0%)
<sup>a</sup> Total group ( $n = 15$ )	13 (86.7%)	2 (13.3%)

	Complete response	Partial response	Stable	Progression
Hormonal				
Mirena $(n = 2)$	1 (50%)	1 (50%)	0 (0%)	0 (0%)
Megace $(n = 3)$	2 (66.7%)	0 (0%)	0 (0%)	1 (33.3%)
Radiation				
External $(n = 2)$	1 (50%)	1 (50%)	0 (0%)	0 (0%)
Brachytherapy	1 (100%)	0 (0%)	0 (0%)	0 (0%)
(n = 2)				
Combination $(n = 2)$	2 (100%)	0 (0%)	0 (0%)	0 (0%)
Chemotherapy	0 (0%)	0 (0%)	1 (00%)	0 (0%)
(n = 1)				
Surgery $(n = 4)$	3 (75%)	1 (25%)	0 (0%)	0 (0%)

<sup>a</sup> 15 of the 21 individuals who received secondary treatment were evaluable. N = 1 individual died post-operatively. N = 2 patients received surgery at outside facilities and records were unavailable at time of data abstraction. Response was not evaluable for N = 1 who received Megace. N = 2 individuals are observed with stable disease after failed initial therapy.

in 74% (n = 17) of patients, and the remaining six (26%) were placed on oral Megace. Median time of maintenance on any initial hormone therapy was 24 (2–92) months. Of the 25 patients who received primary radiation therapy, 14 (56%) underwent a combination of both external beam and brachytherapy, ten (40%) underwent brachytherapy alone, one (4%) underwent external beam therapy alone. There were no major differences among individuals treated with radiation vs. hormonal therapy, respectively, with regard to age (68.4 vs. 64.8, p = .295), BMI (46.1 vs 51.7, p = .109), or number of co-morbidities (3.48 vs. 2.96, p = .289). Of the three patients who initially received concurrent radiotherapy and hormonal therapy, two received brachytherapy alone and one received both brachytherapy and external beam. Mean age for the individuals receiving combination therapy was 58 years, mean BMI was 52.7 kg/m<sup>2</sup> and mean number of comorbidities was 3.67. No one received systemic chemotherapy as primary treatment.

Forty-six patients were evaluable for treatment response. Twentyone (45.6%) individuals required secondary treatment due to persistent or progressive disease. Of those that received hormones initially, response (complete or partial) was seen in 38.1% (n = 8, of 21 evaluable), compared to 63.6% (n = 14, of 22 evaluable) in the radiation group and 100% (n = 3, of 3 evaluable) in the combination group (p = .063). Of the 13 patients who failed to respond to initial hormonal therapy, four were switched to alternative hormonal treatment, four went on to receive radiation alone, one went on to receive radiation followed by a hysterectomy, three went on to have a hysterectomy alone, and one had a hysterectomy followed by adjuvant radiation. One of the five patients treated with hysterectomy after persistent bleeding with hormonal treatment died two days after her surgery while in the Intensive Care Unit due to respiratory failure in the setting of new pulmonary embolism and aspiration pneumonia. Of the eight patients who failed to respond to initial radiation therapy, two were observed with stable disease, two were placed on oral hormonal therapy, three underwent hysterectomy and one underwent chemotherapy for advanced metastatic disease. Of those who received secondary treatment, 87% (N = 13, of 15 evaluable individuals) saw partial response or better. Three individuals requiring secondary treatment were lost to follow-up (one individual who received Megace at an outside facility and two individuals who received a hysterectomy at an outside facility). Of the eight patients ultimately undergoing hysterectomy, there was a 12.5% peri-operative mortality. At time of last follow-up, 32.6% (14 of 43) of evaluable individuals had presence of disease.

Responders and non-responders to initial treatment were compared (Table 3) and there were no significant differences with regard to treatment type, NSQIP scores, BMI, co-morbid conditions or age; however, women with progressive disease following initial therapy were about ten years older (73.9 vs 63.2 years, p = .01), but there was no difference in BMI (48.7 vs 49.7 kg/m<sup>2</sup>, p = .81) or number of co-morbidities (3.4 vs 3.2, p = .72) among individuals with progressive disease and those without, respectively.

Mortality of the cohort was examined and 12 of the 15 deaths were due to a pre-existing co-morbidity rather than a malignancy caused death. Of the remaining three deaths, only one was directly related to her cancer progression. One death was from septicemia following chemotherapy and there was one peri-operative death following robot assisted laparoscopic hysterectomy. The individual who died from cancer progression had papillary serous carcinoma and carcinomatosis with subsequent bowel obstruction.

Mean predicted NSQIP score for risk of death with laparotomy was almost three times as high in individuals who died during this study than in those still living but was not statistically significant (2.7% vs 1.0%, p = .14). Based on NSQIP scores, the predicted complication risk with open hysterectomy was 2.5 times higher than the expected average risk (18.8% vs 7.2%, p < .0001), three times higher for laparoscopic (14.5% vs 5.1%, p < .0001), and death risk was 1–1.5% compared to 0%, p = .003.

# 4. Discussion

For obese patients deemed to have too significant risk of surgical complications, hormone and radiation therapy remain viable options. Among our cohort, 38% of women receiving primary hormonal therapy saw initial response, as well as 64% of women receiving radiation, and 100% of women who received a combination of the two. Even more reassuring; of those requiring secondary treatment due to stable or progressive disease, 87.5% saw partial response or better with subsequent treatment; although the risk of subsequent surgery remained high (1 of 8 women ultimately undergoing surgery died). Our findings add to previous literature supporting the utilization of radiation and hormonal therapy as an alternative in select populations with early

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Table 3

Comparing respon	ders vs non-respon	ders to primary	r treatment.
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Clinical and pathologic characteristics	Response	No response	<i>p</i> -Value
characteristics	n (%) or mean (sd)	n (%) or mean (sd)	
	N = 25	N = 21	
Age (years)	64.7 (11.9)	66.1 (10.8)	0.678
BMI (kg/m <sup>2</sup> )	47.7 (12.6)	51.6 (9.9)	0.255
NSQIP scores			
Risk of complication with laparoscopy	14.1 (4.5)	15.3 (8.0)	0.500
Risk of mortality with laparoscopy	0.8 (0.8)	1.8 (4.9)	
Risk of complication with laparotomy	18.4 (5.6)	19.7 (9.2)	0.270
Risk of mortality with laparotomy	1.1 (1.0)	2.3 (5.6)	0.557 0.282
Number of co-morbidities Race	3.4 (1.4)	3.1 (1.9)	0.549
White	23 (92.0)	16 (76.2)	
Black	2 (8.0)	5 (23.8)	0.137
Presence of specified comorbidity	_ (,	- (,	
Diabetes	14 (56.0)	11 (52.4)	0.806
Hypertension	20 (80.0)	16 (76.2)	0.755
Coronary artery disease	4 (16.0)	3 (14.3)	0.872
Congestive heart failure	7 (28.0)	10 (47.6)	0.225
Hyperlipidemia	8 (32.0)	5 (23.8)	0.744
Asthma/COPD	5 (20.0)	4 (19.0)	0.935
Chronic kidney disease Clinical stage	4 (16.0)	5 (23.8)	0.711
IA	19 (76.0)	15 (71.4)	0.480
IB	2 (8.0)	4 (19.1)	
II	4 (16.0)	2 (9.5)	
Grade			
I	20 (80.0)	20 (95.1)	0.222
II	3 (12.0)	0 (0)	
III	2 (8.0)	1 (4.8)	
Histology			
Endometrioid	24 (96.0)	20 (95.2)	0.362
UPSC	0 (0)	1 (4.8)	
Carcinoma, NOS	1 (4.0)	0 (0)	
Initial treatment	14 (69 6)	0 (0( 1)	0.060
Radiation	14 (63.6)	8 (36.4)	0.063
Hormone therapy	8 (38.1)	13 (61.9)	
Combination	3 (100)	0 (0)	

endometrial cancer. Prior studies report a 5-year overall survival (OS) range of 39 to 71% following primary radiation therapy (Potish et al., 1985b; Varia et al., 1987b; Shenfield et al., 2009b). Most studies represent heterogeneous groups; and many, but not all patients were noted to be obese (BMI  $\geq$  30 kg/m<sup>2</sup>). A case-control study of early stage patients deemed poor operative risk and who were treated by primary radiation therapy and matched to surgically treated controls demonstrated no statistical difference in survival, suggesting that even in patients deemed a poor operative risk, the survival with primary radiation may not be statistically different (Rose et al., 1993). Although, similar to our study, given the small number of patients, true survival statistics are difficult to compare.

Furthermore, a number of retrospective studies have demonstrated high conversion rates to normal endometrium following progesterone treatment in women seeking pregnancy. There are also data supporting the use of intrauterine levonorgestrel for post-menopausal women who are poor surgical candidates, with complete response documented in 50% of patients (Baker et al., 2017). Among individuals treated with hormonal therapy, complete response rates in the postmenopausal patients with the levonorgestrel IUD seem to be comparable to those reported for premenopausal fertility preserving indications (Gunderson et al., 2012; Dorais et al., 2011), albeit endometrial hyperplasia has a significantly higher response to hormonal therapy than endometrial carcinoma. The levonorgestrel IUD and oral Megace were both generally well tolerated within our population of obese, medically ill women.

There are a number of significant limitations in this study, based on its small numbers, retrospective nature, and consequent intrinsic biases. The lack of homogeneity among work-up and treatment modalities makes data interpretation difficult. There was no uniform treatment among patients receiving radiation, nor was there a uniform regimen among patients on oral Megace. Also, assessment of response differed among providers, thus restricting our ability to compare outcomes. Some patients underwent repeat biopsies, some underwent imaging, and others had assessment limited to physical exam alone. In fact, of the 25 individuals in the entire cohort that responded to initial treatment. more than half of them (n = 15, 60%) were deemed to have complete response based on exam alone with no biopsy confirmation and no further imaging performed. Lack of uniform treatment and assessment limits our ability to identify the ideal regimen and duration of therapy. Also, exploring utilization and efficacy of other classes of medication, such as aromatase inhibitors or different generations of progestins will be important. With only two different hormones utilized among our cohort, efficacy comparisons were limited.

Furthermore, there was no uniform utilization of pre-treatment imaging studies, thus restricting our ability to examine the role imaging might play in categorizing ideal candidates for one treatment modality over the other. The decision to avoid surgical intervention in a patient with presumed early stage disease should come fully informed, and pretreatment imaging may be helpful in assessing the presence of extrauterine disease to determine who may benefit from adjuvant chemotherapy. Lastly, true survival statistics are difficult to calculate given the small numbers of patients. Multi-institution collaboration would be ideal to better characterize outcomes and differences among responders and non-responders to help determine ideal candidates for each of the alternative treatment options.

With the rising incidence of obesity and associated co-morbidities in our country, this dilemma will continue to grow more prevalent. Pursuing surgical intervention in this patient population may do more harm than good. Nearly a third of our cohort died, yet only one died from disease progression. The vast majority died from complications of their pre-existing co-morbidities. Special attention should be given to the two individuals who died while receiving treatment for their early stage cancer; including one woman who died two days following a robot-assisted hysterectomy ultimately from post-operative complications and a second woman who was admitted to the hospital while undergoing chemotherapy and ultimately died from septicemia. Unfortunately, these deaths could have potentially been delayed if such perilous measures were avoided but these complications are almost impossible to predict.

Accurate estimation of surgical risk is imperative when considering appropriate treatment options for medically complex obese patients. For some individuals the decision to avoid surgical intervention is obvious, but initial assessment is not always clear-cut. For our cohort, we looked at the ACS NSQIP surgical risk calculator. Although the NSQIP surgical risk calculator has been shown to adequately predict specific serious complications, the overall performance of the calculator may be less accurate in gynecologic oncology patients than reported in general surgery patients, suggesting the need for a tailored prediction model in our population (Rivard et al., 2016). In our small cohort, who were deemed medically inoperable and progressed following initial treatment and were treated surgically, the mortality rate was 12.5% (1/8); again, small numbers limit any conclusions.

As a provider, practicing evidence-based care is how to best assure quality cancer care. However, current data are lacking surrounding management of morbidly obese individuals with early cancer diagnoses. Given our nation's trajectory, development of recommendations for the increasing population of obese, medically complex patients should be prioritized. Based on our data, use of both radiation and hormonal therapy in this patient population is safe and effective. Development and evaluation of a risk calculator specifically for the gynecologic-oncology population would be ideal to help determine which patients would be best suited for pursuing alternative treatments. We were unable to characterize major differences among individuals who responded to treatment and those who did not, likely as a result of our small study size. Thus, further investigation of larger databases would help us better predict who is going to do well and with which treatment modality, so that we can make evidence-based decisions and recommendations.

### Conflict of interest statement

There are no conflicts of interest to disclose.

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