



Using simple radiologic measurements to anticipate surgical challenge in endometrial cancer: a prospective study

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HIGHLIGHTS

- Linear measurements of visceral fat are associated with surgeon-reported difficulty.
- Linear measurements of visceral fat predict difficult surgery better than body mass index.
- Linear measurements of adiposity can easily be obtained from preoperative imaging.

ABSTRACT

Objectives To determine if linear measurements of adiposity from pre-operative imaging can improve anticipation of surgical difficulty among endometrial cancer patients.

Methods Eighty patients with newly diagnosed endometrial cancer were enrolled. Routine pre-operative imaging (MRI or CT) was performed. Radiologic linear measurements of the following were obtained: anterior-to-posterior skin distance; anterior skin to anterior edge of L5 distance (total anterior); anterior peritoneum to anterior edge of L5 distance (visceral obesity); and posterior edge of L5 to posterior skin distance (total posterior). Surgeons completed questionnaires quantifying preoperative anticipated operative difficulty and postoperative reported operative difficulty. The primary objective was to assess for a correlation between linear measurements of visceral fat and reported operative difficulty.

Results Seventy-nine patients had questionnaires completed, preoperative imaging obtained, and surgery performed. Univariate analysis showed all four linear measurements, body mass index, weight, and anticipated operative difficulty were associated with increased reported operative difficulty ($P < 0.05$). Multivariate analysis demonstrated that body mass index and linear measurements visceral obesity and total posterior were independently associated with increased reported operative difficulty ($P < 0.05$). Compared with body mass index, the visceral obesity measurement was more sensitive and specific for predicting increased reported operative difficulty (visceral obesity; sensitivity 54%, specificity 91%; body mass index; sensitivity 38%, specificity 89%). A difficulty risk model combining body mass index, visceral obesity, and total posterior demonstrated better predictive performance than any individual preoperative variable.

Conclusions Simple linear measurements of visceral fat obtained from preoperative imaging are more predictive than body mass index alone in anticipating surgeon-reported operative difficulty. These easily obtained measurements may assist in preoperative decision making in this challenging patient population.

INTRODUCTION

Obesity is a well-established risk factor for the development of endometrial cancer and up to 70% of these patients are overweight or obese.^{1–5} The risk for endometrial cancer increases stepwise with increasing body mass index (body mass index kg/m²) with half of all cases being attributed to excess body weight).^{6,7} Surgeons who care for women with endometrial cancer are frequently confronted with technical challenges from obesity during surgery or the clinical challenges resulting from obesity-related medical comorbidities.

Preoperative decision-making is crucial in this population as obese women with endometrial cancer are at high risk for surgical morbidity.^{2,5,8} In rare cases, the difficulties posed by severe obesity in addition to associated medical complications can make any surgical approach to management highly morbid. Assessing the benefits and risks of pursuing lymph node dissection is a critical part of the preoperative decision-making in managing obese women with endometrial cancer. Obese patients who can safely undergo surgery are less likely to have advanced-stage disease and the benefit of lymph node dissection in low-grade disease is highly debated.^{2,9–13} Lymph node dissection may be omitted if excessive surgical difficulty is anticipated due to obesity, past surgical history, or other patient factors. Before the adoption of sentinel lymph node mapping for endometrial cancer, our institution used an arbitrary body mass index cut-off of 45 kg/m² as a general threshold for anticipated obesity-related surgical difficulty above which lymph node dissection would be performed only if there is preoperative concern for metastatic disease. However, anecdotal experience suggests body mass index is an imperfect predictor of surgical difficulty in obese women.



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First reported in the colorectal surgery literature, measurements of visceral fat have been associated with greater peri-operative morbidity, inferior lymph node retrieval, longer operative time, and more frequent conversion to open surgery.^{14–15} Similar findings have been demonstrated in the urologic and gastric surgery literature.^{16–19} Visceral fat has also been associated with conversion from laparoscopic to open surgery and pulmonary intolerance during robotic surgery in women with endometrial cancer.^{20–21} The aim of this prospective cohort study was to determine if measurements of visceral fat could better anticipate operative difficulty than body mass index calculations in patients undergoing gynecologic surgery for endometrial cancer.

METHODS

The study protocol was approved by the University of Wisconsin Institutional Review Board (ID OS12708). All patients meeting eligibility criteria presenting to our academic gynecologic oncology practice were approached for enrollment. Patients were considered eligible for the study if surgery for endometrial cancer was planned and if they had completed, or could complete, preoperative imaging within 90 days of surgery. This imaging was done as part of an algorithm our institution previously used to triage obese women with endometrial cancer for lymphadenectomy (online supplementary appendix 1).²² Patients were excluded from the trial if they had received prior surgical treatment for endometrial cancer, a history of pelvic radiation, or a surgical history of greater than three laparotomies. Patients unsuitable for surgery due to medical comorbidities were also excluded. Patients provided written informed consent to participate in the trial. Additionally, consent for trial participation was also obtained from the four gynecologic oncologists who would be performing the surgeries and completing preoperative and post-operative assessments of surgical difficulty.

Surgical procedure

Four fellowship-trained gynecologic oncologists participated in this trial. At the discretion of the attending surgeon and consistent with institutional norms, patients underwent a conventional laparoscopic, robotic-assisted laparoscopic, single-incision laparoscopic, or open surgical procedure for endometrial cancer. The route of surgery was at the discretion of the attending surgeon. The surgical team consisted of one attending surgeon with the assistance of a gynecologic oncology fellow, an obstetrics and gynecology resident, or both a fellow and resident.

Linear obesity measurements

Preoperative abdominopelvic CT scan or MRI was performed on all patients within 90 days of surgery. The imaging modality selected was based on the algorithm previously used for the preoperative evaluation of new endometrial cancer patients at our institution (online supplementary appendix 1). All images were electronically transferred to a centralized data system and retrieved at a radiology workstation. Linear adiposity measurements as demonstrated in Figure 1 were collected using McKesson Radiology Station software (McKesson Corporation, San Francisco, CA) (Figure 1). Using the imaging software's built-in measurement features, linear measurements of adiposity were manually determined. These were taken from a mid-sagittal image at the level of the superior endplate

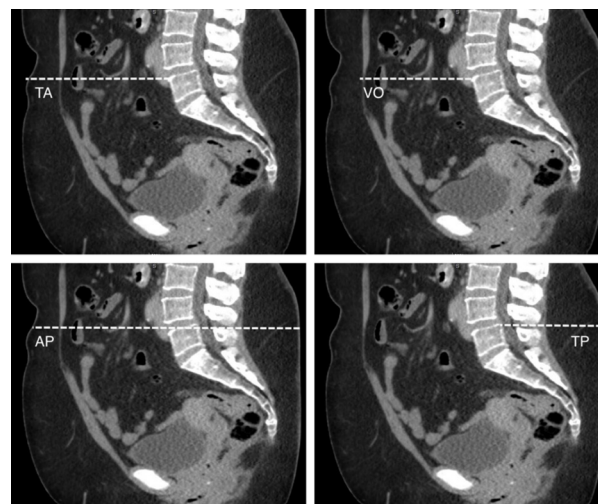


Figure 1 Linear measurements of adiposity. A mid-sagittal image from an abdominopelvic CT scan demonstrating the linear measurements of visceral adiposity; clockwise from top left, the total anterior (TA); visceral obesity (VO); total posterior (TP); and anterior-to-posterior (AP) distances.

(vertebral body) of the fifth lumbar vertebra (L5) perpendicular to the long axis of the body (Figure 1). For the total anterior distance, a measurement was taken from the anterior aspect of the L5 vertebral body to the skin directly anterior to it. The visceral obesity distance was obtained by measuring from the anterior aspect of the L5 vertebral body to the ventral peritoneum anterior to it. The total posterior distance was obtained by measuring from the posterior aspect of the L5 vertebral body to the skin posterior to it. Finally, the anterior-to-posterior distance was obtained by measuring from the ventral-to-dorsal skin edges at the level of L5. All images were reviewed and measurements obtained by a pair of radiologists working together for all patients. These radiologists were not involved in the clinical care of the patients and were blinded to the assessments of operative difficulty completed and surgery performed for each patient.

Assessment of operative difficulty

Each attending surgeon personally completed a preoperative questionnaire after the patient's preoperative clinic visit (online supplementary appendix 2). The first question from that survey tool asked the attending surgeon to numerically quantify how challenging he or she anticipated the planned surgery would be compared with other surgeries of the same type. This rating formed the surgeon's anticipated operative difficulty score. Immediately following surgery, the same attending surgeon would complete a similarly-structured questionnaire quantifying their assessment of surgical difficulty (online supplementary appendix 3). The final question from this postoperative questionnaire asked the surgeon to quantify the difficulty of various aspects of the procedure to a similar surgery of average difficulty. The mean value of the components of the final question on the postoperative questionnaire was used as a reported operative difficulty score. Both the preoperative anticipated operative difficulty and postoperative reported operative difficulty scores were intended to assess surgical challenge in a relative sense compared with other surgeries of the same type, rather than as an absolute measurement of difficulty. The data

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collected from the remaining items on the preoperative and postoperative questionnaires was not included in the final analysis for this study. Since a review of the published literature did not identify a validated tool to assess a surgeon's perception of operative difficulty, these surveys were developed specifically for this trial by the authors with input from the four participating surgeons. Operative time, surgical blood loss, conversion to open surgery, and surgical complications were ascertained by retrospective chart review. The attending surgeon were blinded to the linear adiposity measurements when completing pre- and postoperative questionnaires.

Statistical analysis

Since there was a lack of preliminary data available on which to base a sample size calculation, a cohort of 80 patients was proposed based on the anticipated number of patients expected to be accrued within 1 year. Our primary outcome of interest was to determine if increasing linear adiposity measurements, as described above, were correlated with higher reported operative difficulty scores on the postoperative questionnaires. Our secondary outcome was to determine if these measurements were associated with higher reported operative difficulty scores independent of body mass index on multivariate analysis. Finally, we sought to determine if the measurements could predict reported operative difficulty scores more accurately than body mass index. The Pearson correlation coefficient was used to evaluate the association of preoperative variables and visceral fat measurements with reported operative difficulty. All computations were performed using the R statistical language version 3.0.2. P-values for univariate associations were attained by ordinary least squares. All t-tests were the two-sample versions with equal variances.

RESULTS

Patient characteristics, surgical data, and linear adiposity measurements are presented in Table 1. A total of 80 patients enrolled in the study within the course of a year. After enrollment, one patient did not undergo surgery due to extensive metastatic disease observed on preoperative imaging. The remaining 79 patients who had preoperative imaging reviewed, pre- and postoperative questionnaires completed, and surgery performed were included in the final analysis. There were 61 patients (76%) who were obese (body mass index >30 kg/m²). Mean body mass index of the study population was 37.7 kg/m² (range 18.7–59.1 kg/m²).

The majority of cases were performed using a minimally-invasive approach (69; 87%). Most patients had a tumor of endometrioid histology (79.7%) and early stage disease (74.7%). Mean operative time was 195 min (range 90–314). Mean estimated surgical blood loss was 178 mL. Lymph node dissection was performed in 39 cases (49%) with an average lymph node yield of 10 per case (range 1–44). Significant surgical complications occurred in four patients (5%): there were two cystotomies, one enterotomy, and one inferior vena cava laceration. Conversion from a planned minimally invasive approach to laparotomy occurred in five patients (7%). The preoperative and postoperative questionnaire results are presented in Table 2. Mean and median anticipated operative difficulty score was found to be 4.5 and 5 (range 2–7; interquartile range 4–5), respectively. Mean and median reported operative difficulty score

Table 1 Patient demographics, surgical data, and linear adiposity measurements

| Variable | Value |
|------------------------------------|---------------------------------------|
| Demographics | |
| Age, y | 61 (33–86) |
| Height, m | 1.6 (1.4–1.8) |
| Weight, kg | 99.2 (52–160) |
| BMI, kg/m ² | 37.7 (18.7–59.1) |
| Surgical data | |
| Technique, n (%) | |
| Robotic-assisted | 49 (62%) |
| Laparoscopy | 13 (16%) |
| Planned laparotomy | 7 (10%) |
| Single-incision laparoscopy | 10 (12%) |
| Operative time, min | 195 (90–314) |
| Estimated blood loss, mL | 178 (5–1500) |
| Lymphadenectomy performed, n (%) | 39 (49%) |
| Intraoperative complication, n (%) | 4 (5%) |
| Conversion, n (%) | 5 (7%) |
| Lymph nodes sampled, n | 10 (1–44) |
| Histology | |
| Endometrioid | 63 (79.7%) |
| Carcinosarcoma | 3 (3.8%) |
| Serosus | 2 (2.5%) |
| Benign* | 6 (7.6%) |
| Other† | 5 (6.3%) |
| Stage | |
| I | 59 (74.7%) |
| II | 8 (10.1%) |
| III | 5 (6.3%) |
| IV | 1 (1.2%) |
| N/A‡ | 6 (7.6%) |
| Linear adiposity measurements | |
| | Mean Median Range IQR |
| Skin-to-skin, cm | 30 30 17–46.7 24.5–34.4 |
| Total anterior, cm | 15.7 15.8 6.5–26.4 12.0–18.8 |
| Visceral obesity, cm | 11.3 11.3 4.3–22 8.1–14.1 |
| Total posterior, cm | 11.1 10.8 5.9–26.6 9.5–12.5 |

Mean values are followed by range in parentheses, unless otherwise indicated.

*Benign final pathology after preoperative biopsy showed carcinoma.

†Two cases mixed histology; two cases undifferentiated histology; one case neuroendocrine histology.

‡Benign cases.

BMI, body mass index; IQR, Interquartile Range.

was found to be 3.8 and 4.2 (range 1–6.4; interquartile range 2.8–4.8), respectively.

Significant correlations were observed between all linear measurements and the reported operative difficulty score (Table 3). Additionally, the surgeon's anticipated operative difficulty score, body mass index, and weight were also found to be significantly correlated with an increased reported operative difficulty score.

Table 2 Anticipated and reported operative difficulty scores

| Variable | Mean | Median | Range | IQR | Cases (n, %) |
|------------|------|--------|---------|---------|--------------|
| Surgeon 1* | | | | | 11 (14%) |
| AOD score | 4.1 | 4 | 3–5 | 4–4.5 | |
| ROD score | 2.6 | 2.8 | 1–4 | 1.8–3.6 | |
| Surgeon 2† | | | | | 31 (39%) |
| AOD score | 4.6 | 5 | 1–7 | 4–6 | |
| ROD score | 4.1 | 4.3 | 1.3–6.4 | 3.1–5.2 | |
| Surgeon 3‡ | | | | | 25 (32%) |
| AOD score | 4.3 | 4 | 2–7 | 3–5 | |
| ROD score | 3.6 | 4 | 1–5.7 | 2–5 | |
| Surgeon 4§ | | | | | 12 (15%) |
| AOD score | 5.1 | 5 | 1–6 | 5–6 | |
| ROD score | 4.1 | 4.4 | 1.8–5.4 | 4–4.5 | |
| Cohort | | | | | 79 (100%) |
| AOD score | 4.5 | 5 | 2–7 | 4–5 | |
| ROD score | 3.8 | 4.2 | 1–6.4 | 2.8–4.8 | |

Anticipated operative difficulty and reported operative difficulty scores were reported on a range of 1 to 7, with higher scores representing greater than typical degrees of difficulty.

*AA

†DK

‡LB

§SR

AOD, Anticipated operative difficulty; IQR, Interquartile Range; ROD, Reported Operative Difficulty.

After multivariate analysis, only body mass index, the visceral obesity measurement, and total posterior measurement remained significantly correlated with an increased reported operative difficulty score (Table 4). The visceral obesity measurement demonstrated a stronger correlation with the reported operative difficulty score compared with BMI.

Using the variables found to be independently associated with increased reported operative difficulty after multivariate analysis, a difficulty risk model (DRM) was developed:

$$DRM = 1.56 + (0.0833 \times BMI) + (0.142 \times VO) - (0.231 \times TP)$$

This model's predicted difficulty score was more strongly correlated with an increased reported operative difficulty score than body mass index alone (DRM $R^2=0.54$; BMI $R^2=0.38$ [$P<0.0001$])

or the other individual variables that composed the difficulty risk model.

As described above, our institution previously used a body mass index measurement of 45 kg/m² as an arbitrary threshold for anticipated surgical difficulty above which lymph node dissection would not be performed unless there was preoperative concern for metastatic disease. Based on the correlation between body mass index and the reported operative difficulty score ($R^2=0.38$), a body mass index cut-off value of 45 kg/m² would correspond to an expected reported operative difficulty score of 4.43. In our cohort, this body mass index cut-off would correctly anticipate 38% of the truly difficult cases (ie, reported operative difficulty score ≥ 4.43) as difficult and correctly anticipate 89% of non-difficult cases (ie, reported operative difficulty score < 4.43) as not difficult. Using the difficulty risk model and this body mass index cut-off value, corresponding cut-off values for the visceral obesity measurement and

Table 3 Variables correlated with increased reported operative difficulty score, univariate analysis

| Variable | R value | P values |
|------------------------------|---------|----------|
| Total posterior measurement | 0.31 | 0.0046 |
| Weight | 0.52 | <0.0001 |
| BMI | 0.6 | <0.0001 |
| Skin-to-skin measurement | 0.6 | <0.0001 |
| AOD score | 0.62 | <0.0001 |
| Visceral obesity measurement | 0.63 | <0.0001 |
| Total anterior measurement | 0.67 | <0.0001 |

AOD, anticipated operative difficulty; BMI, body mass index.

Table 4 Variables independently correlated with increased reported operative difficulty score, multivariate analysis

| Variable | Estimated coefficient | Std. error of coefficient | P values |
|------------------------------|-----------------------|---------------------------|----------|
| Total posterior measurement | −0.231 | 0.082 | 0.0063 |
| BMI | 0.083 | 0.021 | 0.00019 |
| Visceral obesity measurement | 0.142 | 0.037 | 0.0023 |

BMI, body mass index.

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Table 5 Performance of predictive variables for anticipating difficult surgery

| Predictive variable | Cut-off value | Sensitivity | Specificity |
|------------------------------|----------------------|-------------|-------------|
| BMI | 45 kg/m ² | 38% | 89% |
| Visceral obesity measurement | 14.3 cm | 54% | 91% |
| DRM | 4.43 | 62% | 93% |

BMI, body mass index; DRM, difficulty risk model.

difficulty risk model score were determined and compared with the predictive performance of body mass index for anticipating difficult surgeries defined as a reported operative difficulty score ≥ 4.43 . The cut-off visceral obesity measurement was calculated to be 14.3 cm based on correlation between the visceral obesity measurement and reported operative difficulty score determined previously. When compared with the predictive performance of a cut-off body mass index value of 45 kg/m², a visceral obesity measurement of ≥ 14.3 cm was better at anticipating difficult and non-difficult surgeries (visceral obesity ≥ 14.3 cm: sensitivity, 54%; specificity 91%; body mass index ≥ 45 kg/m²: sensitivity, 38%; specificity 89%) (Table 5). The difficulty risk model score, which incorporates body mass index and the visceral obesity measurement as well as the total posterior measurement in its calculation, displayed better predictive performance for anticipating difficult and non-difficult surgeries than either of the individual component variables (DRM score ≥ 4.43 : sensitivity 62%; specificity 93%).

COMMENT

This prospective study demonstrates that linear measurements of visceral fat from preoperative imaging predict operative difficulty better than body mass index in patients undergoing surgery for endometrial cancer. Surgeons can use these linear measurements to aid in preoperative decision-making. As an example, the decision to pursue lymph node dissection in an obese patient with endometrial cancer is a complex one. Obese patients with low-grade endometrial cancer are less likely to have advanced-stage disease.² Lymph node assessment, whether in the form of lymph node sampling, sentinel lymph node mapping, or comprehensive lymphadenectomy, may change treatment decisions but has not itself been associated with therapeutic benefit. Obese patients are at increased risk for surgical morbidity relative to their normal weight peers, and the decision to pursue lymph node dissection has direct implications on the length, extent, and risk of surgery for these patients. Preoperative assessment of surgical difficulty can aid in making decisions related to lymphadenectomy and is a potentially added benefit from the standpoint of resource allocation and informed treatment planning. Our results indicated that visceral adiposity measurements can add to the surgeon's ability to anticipate surgical difficulty.

This study further reveals that linear visceral fat measurements are predictors of operative difficulty independent of body mass index. These findings build on previously published studies in the endometrial cancer literature that examine the use of visceral fat in predicting perioperative outcomes.^{20 21} Prior reports have associated increased visceral fat with greater risk of conversion

to laparotomy as well as poor pulmonary tolerance to pneumoperitoneum during robotic surgery.^{20 21} The linear measurements described in this study can easily be obtained from preoperative imaging studies using tools available on most standard radiology imaging interfaces.

Our data allowed us to develop a difficulty risk model that incorporated the variables we found to be independent predictors of reported operative difficulty, specifically body mass index, the visceral obesity measurement, and the total posterior measurement. This model reveals that if body mass index and the total posterior measurement are fixed, each 1 cm increase in the visceral obesity measurement corresponds to an increased operative difficulty of 0.14 points on a 7-point difficulty scale. Interestingly, when body mass index and the visceral obesity measurement are fixed, each 1 cm increase in the total posterior measurement predicts a decrease in the operative difficulty of 0.23 points on the same scale. Stated differently, for patients with similar body mass indexes, greater visceral fat within the peritoneum predicts harder surgery, whereas more fat posterior to the spine predicts a less difficult surgery. The finding that intraabdominal adiposity results in more difficult surgery is understandable, as intraabdominal fat obscures surgical anatomy and impairs visualization. We were surprised to find that greater adiposity posterior to the spine predicts less difficult surgery. It is possible that this observation may reflect individual differences in patient body shapes and relative distributions of fat. For example, in patients with similar body mass indexes, a patient with greater adiposity posterior to the spine may have less intraabdominal adiposity.

There are several important limitations of the study. Most notably, surgeon-reported difficulty is an inherently subjective outcome as opposed to objective, surrogate markers for difficulty such as operative time, estimated blood loss, or lymph node yield. In a secondary analysis, we found that operative time was correlated with a higher reported operative difficulty score ($R=0.61$; $P<0.05$). Future studies with a larger sample size may allow for the investigation into any relationship between linear visceral fat measurements and clinically-relevant, objective outcomes in endometrial cancer surgery. We decided to not limit the surgical approach performed by the surgeon to any single modality. As a consequence of this, the number of surgeries performed by any single approach for any individual surgeon is relatively small. We did not account for how a surgeon's impression of difficulty may vary between surgical approaches. Further, the surgical difficulty data is based on the impressions of only four surgeons. We did not account for interobserver variability among the surgeons. However, the questionnaire was designed to rate surgical difficulty relative to what was expected for a similar procedure, rather than to assess difficulty in an absolute sense. The study was performed at a single institution and the study population was ethnically homogeneous, as there was only one non-white participant. This may limit the generalizability of the study, as fat distribution varies among different ethnic groups.²³ The linear measurements were obtained from either MR or CT based on institutional norms for the preoperative evaluation of new endometrial cancer patients rather than a standardized imaging modality for this study.

Prior studies have quantified visceral fat using visceral fat areas, where computer software calculated the area of intraabdominal fat from single-cut CT images at a predetermined level in the abdomen.

In this study, we selected linear measurements due to the ease of use and accessibility. Most radiology workstations allow for simple linear measurements to be made by the surgeon from preoperative imaging. Visceral fat area determinations require specialized software and technical expertise. With the hope of developing a more clinically accessible tool, we elected to use a simple measurement of visceral fat, although one that is different from previously described methods.

To conclude, linear measurements of adiposity, especially visceral obesity, better anticipate operative difficulty in patients undergoing surgery for endometrial cancer rather than body mass index itself. Using standard imaging review software, a surgeon can easily obtain, for example, the visceral obesity measurement by taking a linear measurement of the distance between the L5 vertebral body and the ventral peritoneum anterior to it in the midline. Using these measurements, the surgeon has a new tool for anticipating operative difficulty that we found performs better than body mass index at predicting surgical challenge. Better foresight of operative difficulty prior to surgery may aid preoperative decision-making in a population at high risk for surgical morbidity. Difficult decisions, such as those pertaining to lymph node assessment or whether to avoid surgery altogether, are common in this patient population. Improved anticipation of surgical challenge with these linear measurements can be beneficial to the decision-making process.

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