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Overweight and obese women's symptoms, knowledge, and preferences regarding endometrial biopsy for endometrial cancer detection: A threshold technique survey

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ABSTRACT

Background: The incidence of endometrial cancer (EC) in the United States continues to rise, driven mainly by the obesity epidemic. We sought to determine overweight and obese women's cancer risk knowledge and preferences regarding diagnostic endometrial biopsy (EMB) for EC detection.
Methods: An online survey was administered to overweight and obese women without EC recruited through the electronic medical record's online patient portal. Baseline questions queried gynecologic history, cancer risk knowledge, and factors potentially influencing decision-making for EMB. We used the threshold survey technique to identify the minimum acceptable risk (MAR) threshold at which each respondent would be willing to undergo an EMB to detect EC.
Results: Of 357 respondents (median age 45 years (interquartile range [IQR]: 38–54; median BMI 39 [IQR: 36.0–44.6]), fewer than half (48.7 %) were aware that obesity is a risk factor for EC, and 10 % considered their risk of EC to be high. Almost half (42 %) of respondents reported MAR thresholds characterized as very low (0–1 %), and these were more common among respondents with higher BMIs. Forty percent identified their weight as a factor influencing their MAR threshold decision, while 76 % identified their perceived personal risk as a factor. Less than half cited immediate risks of the procedure.
Conclusion: Many patients reported being willing to undergo an EMB at very low risk thresholds for EC. Perceived personal risk is a stronger factor in decision-making than immediate procedural risks. Providers should focus on communicating patients' risk to motivate EMB to detect EC where appropriate.

1. Background

Endometrial cancer (EC) incidence rates in the United States are rising in part due to the obesity epidemic. Approximately 50% of new EC cases are directly attributable to obesity (Calle and Overweight, 2004; Onstad et al., 2016). Most patients with EC present with early-stage disease and symptoms of abnormal uterine bleeding (AUB), ranging from heavy and inter-menstrual bleeding in premenopausal women to any post-menopausal bleeding. Many patients, however, do not recognize their bleeding symptoms as abnormal, leading to delayed diagnosis

and treatment. For example, most women presenting to a multidisciplinary clinic report AUB symptoms, but only 60% had discussed these symptoms with a gynecologist. (Beavis et al., 2020) In another study of female patients presenting for bariatric surgery who underwent empiric endometrial biopsy, 14% had undiagnosed EC or atypical hyperplasia, a precursor to EC (MacKintosh et al., 2019).

Endometrial sampling is standard for postmenopausal women with bleeding, patients older than 45 years with AUB, and patients younger than 45 with persistent AUB, a history of unopposed estrogen exposure (e.g., obesity or polycystic ovary syndrome), or failed medical

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management (Practice bulletin no. 128, 2012). However, there are currently no EC screening recommendations for women who are not at elevated genetic risk, and early detection relies on prompt recognition of atypical bleeding symptoms by both provider and patient. While endometrial biopsies (EMB) offer a simple, in-office opportunity for sampling of the endometrial lining that is both sensitive and specific for detecting EC, they can be painful and anxiety-producing for patients (Kaiyrlykyzy et al., 2021). Delineating the barriers to having a diagnostic workup (e. g., EMB) for EC among women at risk necessitates understanding patient perspectives of that workup. Therefore, we conducted this survey study to investigate obese women's perceptions of EC risk, evaluate the risk threshold at which they would undergo EMB, and the factors that influence that decision-making.

2. Methods

2.1. Patient Recruitment

The Johns Hopkins Institutional Review Board approved this survey-based study. Respondents were recruited through a secure electronic invitation sent via the online patient portal (MyChart) within the electronic medical record (Epic). Recruitment messages were sent to patients aged 30 to 65 who had received care at Johns Hopkins within the last year and a most recently recorded BMI of at least 35 (to enrich for higher levels of obesity). Electronic recruitment messages were sent out daily until a target of 400 completed surveys, at which time the online survey was deactivated. Per institution protocol, patients who had previously opted out of electronic research recruitment messages were not eligible to receive messages.

2.2. Survey design and development

The survey included questions addressing gynecologic and menstrual history and evaluated the respondents' knowledge of obesity and cancer risk, similar to our prior study (Beavis et al., 2020). We also included questions that assessed the respondents' perceived personal risk of EC, the threshold of EC risk at which the participant would undergo an EMB to detect EC, and factors that influenced their decision-making when choosing that threshold (see Appendix 1 for the full survey instrument). We utilized the threshold technique - a survey technique commonly used to quantify the willingness of patients to undergo medical treatments or procedures (Hauber and Coulter, 2020) – to determine the minimum acceptable immediate risk (MAR) of EC at which the patient would agree to undergo EMB. Preceding the description of an EMB and subsequent series of threshold questions, we included an informational statement: "Women who are overweight are more likely to develop endometrial pre-cancer or cancer" (respondents were not able to return to knowledge questions at this point in the survey). The description of the EMB was accompanied by a depiction of the procedure, coupled with estimates of associated risks, including discomfort, infection (less than 1/100 chance), and uterine perforation (1/1000 chance). The benefits of endometrial biopsy were also described, namely the high sensitivity (approximately 95 %) in detecting EC.

Then, patients were asked, "If the chance that you have endometrial cancer right now is 100 %, would you want to undergo an endometrial biopsy to detect it?"; if the participant answered affirmatively, we asked the same question with sequentially lower and more nuanced levels of risk: 50%, 40%, 30%, 20%, 15%, 10%, 5%, 2.5%, 1%, 0% until the respondent answered "no". The risk threshold was categorized as the lowest percentage at which the participant would be willing to undergo biopsy (e.g., if "yes" to 5% but "no" to 2.5%, MAR threshold is 5 %). To improve understandability, chance was presented in both percentages (e.g., 50%) and fractions (e.g., 1 in 2 chance).

Respondents were then asked to reflect on their decision-making during the threshold questions and state their level of agreement with statements that identified possible decision-influencing factors, including personal and procedural factors.

During survey development, we conducted eight cognitive interviews (Willis and Artino, 2013) to optimize the readability and understandability of survey questions and pilot-tested the survey with 11 additional individuals. The final survey consisted of a maximum of 51 questions and took 7–10 min to complete. Respondents were compensated $25 for cognitive interviews, $10 for pilot testing, or $8 for completion of the final survey.

2.3. Statistics

Respondents who self-reported a history of uterine or cervical cancer, a heritable EC syndrome, hysterectomy, age < 30 or > 65, or with BMI < 25 or unknown were excluded from analyses. We used descriptive statistics to report continuous variables (median and interquartile range [IQR]) and categorical variables. We created a composite variable for AUB in premenopausal women (including heavy or irregular and/or prolonged cycles.).

For Likert scale questions of agreement, three categories were identified: agree (responses: strongly agree/agree), unsure/neutral, and disagree (responses: disagree, strongly disagree); for questions of obesity and increased cancer risk, answers of "a lot" or "a little" were both considered affirmative responses.

Primarily guided by participant-reported MAR thresholds, we categorized respondents into three categories of MAR level: very low MAR (risk threshold 0–1%), low MAR (risk threshold 2.5–30%), and high MAR (risk threshold 40–100%). We used Chi-squared tests of association to test if these levels of MAR differed by age (<51 vs. ≥ 51 years), race (Black vs. white/other), self-reported BMI (25–39.9, 40–49.9, and ≥ 50 kg/m^2), and reported history of D&C or EMB. Fewer than 5% of questions were missing/left blank; these responses were excluded from calculations, and missingness is described throughout the results. All analyses were performed at a 0.05 level of statistical significance. Stata 18 statistical software program was used to perform statistical analyses.

3. Results

3.1. Demographics and gynecologic history

A total of 2,828 invitations were sent before the target of 400 repsondents was reached. Three hundred and fifty seven respondents met criteria for inclusion in analyses. The median age was 45 years (IQR: 38–54), and the median self-reported BMI was 39.0 kg/m^2 (IQR 36.0–44.6) (Table 1). Fifty-two percent (n-184) of respondents were White, and 37.3 % (n = 133) were Black or African American. Data on invitees who did not respond to the survey invitation were not available for analysis.

Almost all respondents (98.0 %, n = 350/357) reported having had a Pap smear in the last five years, and 69.5 % had visited a gynecologist in the last year. Forty percent (n = 141) had undergone an EMB or D&C previously. Amongst the 207 premenopausal women who reported having a period in the last year, 58 % (n = 120) reported at least one AUB symptom.

3.2. Cancer knowledge and perceived EC risk

Approximately half of the respondents correctly identified obesity as a risk factor for breast cancer (56.9 %, n = 202/355 with non-missing data), colon cancer (57.5 %, n = 204), and endometrial cancer (48.7 %, n = 173) (Fig. 1). Only 17.1 % (n = 63) and 28.2 % (n = 100) correctly identified that obesity is *not* a cervical and lung cancer risk factor, respectively. Ten percent (n = 38) of women strongly agreed or agreed that "My chances of getting endometrial cancer in the next few years is high", while 37.2 % (n = 132) disagreed with the statement, and 52 % (n = 185) were uncertain if their risk was high or not.

Table 1

Demographic characteristics and gynecologic history of survey respondents (n = 357).

Demographics		
Age, median (IQR)	45	(38–54)
	N	(%)
Body mass index (BMI) in kg/m2		
<30	4	(1.1)
30-<35	55	(15.4)
35-<40	135	(37.8)
40-<50	121	(33.9)
≥50	42	(11.8)
Highest level of education		
High school or less	143	(40.1)
College/vocational	87	(24.4)
Graduate degree	111	(31.1)
Not stated	16	(4.5)
Self-reported race		
White	184	(51.5)
Black	133	(37.3)
Asian	6	(1.7)
More than one of the above	6	(1.7)
Other, prefer not to answer	28	(7.8)
Gynecologic History		
History of endometrial biopsy or D&C (ever)	141	(40.4)
Reported visit with gynecologist in past 12 months	248	(69.5)
Reported Pap smear in the last 5 years	350	(98)
Menopausal status*		
Self-reported pre-menopausal with a period in the last 12 months	207	(58.0)
Amenorrheic, but respondent denies being postmenopausal	41	(11.5)
Amenorrheic, but respondent unsure if postmenopausal	12	(3.4)
Self-reported postmenopausal	96	(27.0)

3.3. MAR threshold & factors influencing decision-making

The most frequently reported MAR threshold to undergo EMB was 1 %, reported by 28.8 % of respondents (n = 101/351 with non-missing data, Fig. 2).

The next most common threshold was 0% (indicating they would desire a biopsy even if personal risk was 0%), reported by 13.1% (n = 46). Thirty-five percent (n = 124) were categorized as having a low MAR (range 2.5–30%), and 22.8% (n = 80) had a high MAR (range 40–100%). MAR level category differed by BMI: MAR threshold was lower in those with higher BMIs (Table 2). MAR threshold did not differ by age, race, history of EMB or D&C, or perceived EC risk (supplementary tables S1A-S1D).

The most commonly reported decision-influencing factor was their perceived personal risk of developing EC (75.9 %, n = 261/344; Table 2). Personal weight was reported as a factor for only 40.4 % (n = 139) of respondents. Immediate risks associated with the procedure were also cited by approximately half of the respondents, including pain (43.9 %, n = 151), infection (44.2 %, n = 152), and uterine perforation (50.9 %, n = 175). Time to complete the procedure was infrequently reported as a factor (n = 71, 20.6 %).

4. Discussion

In this survey of 357 overweight and obese women, only half of the respondents correctly identified obesity as a risk factor for EC. Only 10 % of respondents perceived their EC risk as high. Respondents were, however, willing to undergo diagnostic EMB at low levels of risk, with the most frequently cited MAR threshold of 1 %. Perceived personal risk (but not personal weight) was commonly cited as a decision-influencing factor. These results provide insight into patient perspectives that could help inform counseling at-risk patients.

Our study is consistent with previously published surveys demonstrating that patients have poor knowledge of the relationship between cancer and obesity (Soliman et al., 2008; Wilkinson et al., 2020). Our results support the need for improved education on the risks of EC with obesity. Similar to other studies, we also found that AUB – a common symptom of EC - was frequently reported amongst premenopausal respondents. Other studies have further demonstrated that patients often do not discuss their symptoms with their provider. Even when providers are made aware, they may not adhere to diagnostic biopsy guidelines, particularly in premenopausal women (Beavis et al., 2023; Cordasco et al., 2019). Our results suggest that many patients would be willing to undergo EMB if offered. These findings, coupled with the projection that the incidence of EC will increase by 55 % by 2030 (Sheikh et al., 2014), magnify a critical need to educate providers and patients to improve early detection of EC through prompt endometrial sampling.

Guidelines state that the decision to perform an EMB in a patient should be based on risk factors for EC. However, there is no physician and guideline endorsed exact percentage risk at which biopsy is universally recommended. In postmenopausal women with bleeding, the EC risk ranges from 1 to 14 % and biopsy is almost always recommended (ACOG Committee Opinion No, 2018). In premenopausal women with AUB, immediate hyperplasia or EC risk may be as low as 1–2 % or as high as 35 % when accounting for groups of risk factors. The patients in our study were willing to undergo a diagnostic biopsy to detect EC even if their immediate risk was very low – 1 %. While these risk levels seem very low, in cognitive interviews, we did find that interviewee's chose a MAR of 0 % for fear that there was still some residual risk they could have EC. Another study of patients with Lynch syndrome found that biannual biopsy was acceptable, with a *lifetime* risk of 20 %. (Sun et al., 2019) Ultimately, future research is needed to estimate individual risk better and identify a patient- and provider-acceptable
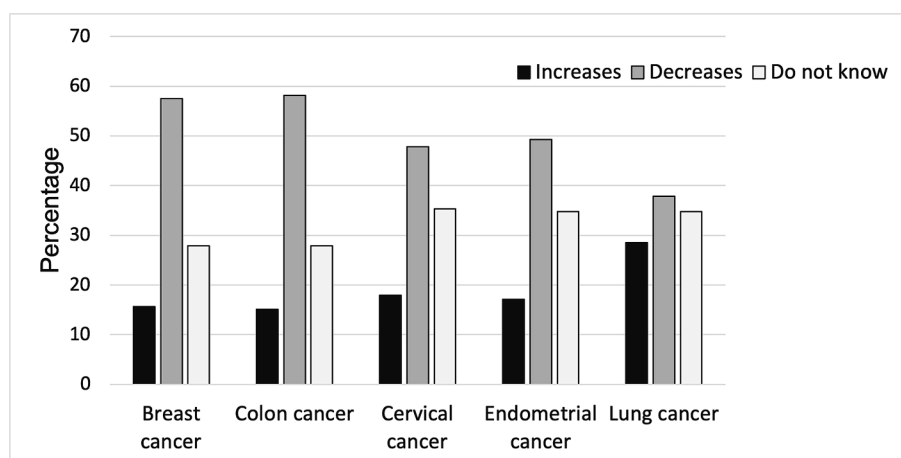

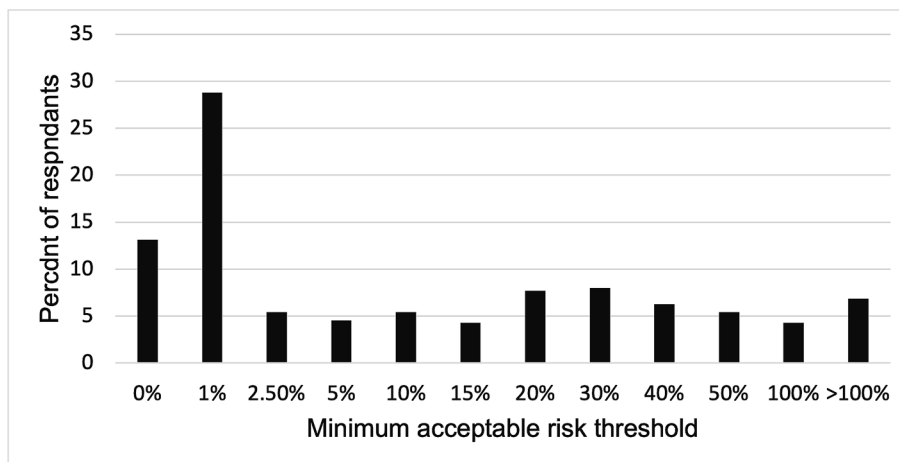**Fig. 1.** Participants responses to knowledge questions of obesity and impact on cancer risk.

Fig. 2. Percent of patients identifying each risk threshold level at which they would be willing to undergo endometrial biopsy.

Table 2
Percent of respondents categorized as having very low, low, and high minimum acceptable risk (MAR) of endometrial cancer at which they would undergo an EMB, stratified by body mass index (BMI). Global Chi square test of association p-value = 0.01.

	All		BMI 25–39.9		BMI 40–49.9		BMI ≥ 50	
	N	(%)	N	(%)	N	(%)	N	(%)
Very low MAR (0–1 %)	147	(41.9)	72	(37.5)	51	(43.2)	24	(58.5)
Low MAR (2.5–30 %)	124	(35.3)	82	(42.7)	35	(29.7)	7	(17.1)
High MAR (40–100 %)	80	(22.8)	38	(19.8)	32	(27.1)	10	(24.4)

*Missingness n = 13, 2.0 %;

threshold at which to offer EMB for EC detection.

Our study provides insight into the motivating and influencing factors of patients at elevated risk of EC. Our findings suggest that respondents' understanding of their personal risk of malignancy appears to drive their decision-making. Additionally, fewer than half of patients identified their weight as a decision-influencing factor, but higher BMI was associated with lower MAR thresholds. Providers should focus counseling on explaining why the individual patient is at higher risk to motivate patients to undergo EMB, where appropriate.

Strengths of the study include the rigorous survey development and diverse sample of patients with a wide range of educational backgrounds, age, BMI, and race. Limitations of this study are inherent to survey-based techniques and include both response and selection bias. Further, 40 % of respondents had previously undergone an endometrial biopsy or dilation and curettage, and results may not reflect women who have never had endometrial sampling. Our interpretation of results with respect to endometrial sampling is also limited by the fact that we did not ask the indication for this sampling, or if it was performed in-office or under anesthesia.

Our study suggests patients are motivated to undergo EMB even at low EC risk, and counseling should focus on each individual patient's risk factors. Future studies should focus on developing and implementing tools that aid patient-provider communication and decision-making regarding EC risk. These tools can help providers identify those patients at highest risk in order to target endometrial sampling and maximize early EC detection.

CRediT authorship contribution statement

Anna L. Beavis: . **Zishan Hirani:** Writing – review & editing, Visualization. **Tullia Rushton:** Writing – review & editing, Visualization, Investigation. **Mary Catherine Rush:** Writing – review & editing, Writing – original draft, Project administration, Data curation. **Amanda N. Fader:** Writing – review & editing, Funding acquisition. **Gayane Yenokyan:** Writing – review & editing, Formal analysis. **Anne F. Rositch:** Writing – review & editing, Supervision, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

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

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gore.2024.101361.

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