Patient acceptance of transvaginal sonographic endometrial thickness assessment compared with hysteroscopy and biopsy for exclusion of endometrial cancer in cases of postmenopausal bleeding

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ABSTRACT

Introduction: Available examinations for women with postmenopausal bleeding include transvaginal sonography to measure endometrial thickness (TVS-ET), and invasive endometrial assessment using hysteroscopy/endometrial biopsy. However, selection of the examination method seldom involves consideration of patient preferences. The aim of this study was to examine patient preferences for the method used to investigate postmenopausal bleeding.

Methods: Women were asked to complete an interviewer-administered structured survey before they underwent clinical investigations at a university gynaecology unit from June 2016 to June 2017. Using the standard gamble approach, women were asked to choose between invasive assessment by hysteroscopy/endometrial biopsy (gold standard) or TVS-ET with a risk of missing endometrial cancer. The risk of missing endometrial cancer during TVS-ET was varied until each woman was indifferent to either option.

Results: The median detection rate for endometrial cancer required using TVS-ET was 95% (interquartile range=80%-99.9%). In total, 200 women completed the survey, and 77 (38.5%) women required TVS-ET to have a 99.9% detection rate for endometrial cancer. Prior hysteroscopy experience was the only factor that influenced the women's decisions: a significantly higher detection rate was required by this patient group than by patients without previous hysteroscopy experience (P=0.047).

Conclusion: A substantial proportion of women would accept TVS-ET alone for the investigation of postmenopausal bleeding. In the era of patient-centred care, clinicians should incorporate patient preferences and enable women to make informed choices concerning the management of postmenopausal bleeding.

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New knowledge added by this study

- We assessed patient preferences for the investigational approach used to exclude endometrial cancer in Hong Kong women with postmenopausal bleeding.
- In our study population, most women would select transvaginal sonography to measure endometrial thickness (TVS-ET) if the endometrial cancer detection rate were >95%; if the TVS-ET detection rate were ≤95%, the women would select the more invasive hysteroscopy/endometrial biopsy approach.
- Nearly 40% of the women required TVS-ET to detect nearly all endometrial cancers before they would select TVS-ET as the sole investigational approach.

Implications for clinical practice or policy

- Using an endometrial thickness cut-off value of 3 mm, a substantial proportion of women would accept TVS-ET alone for the investigation of postmenopausal bleeding.
- Women with previous hysteroscopy experience prefer hysteroscopic assessment unless TVS-ET alone can achieve a nearly identical rate of endometrial cancer detection.
- Clinicians should incorporate patient preferences concerning the investigation of postmenopausal bleeding to enable an informed choice about invasive testing to exclude endometrial cancer.

絕經後出血患者對經陰道超聲波測量子宮內膜厚度評估相比宮腔鏡檢查和活檢排除子宮內膜癌的接受程度

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引言：絕經後出血患者的檢查包括經陰道超聲波檢查以測量子宮內膜厚度（TVS-ET），以及使用宮腔鏡／子宮內膜活檢進行侵入性子宮內膜評估。然而，制定檢查方案時很少考慮到患者的選擇。本研究旨在對患者的絕經後出血評估方案選擇作出探討。

方法：2016年6月至2017年6月期間，絕經後出血患者在教學醫院婦科接受臨床檢查前被邀請參加面談式研究調查。透過標準博弈法為基礎，研究人員以遞減TVS-ET有漏診子宮內膜癌的風險數值，探討患者對非侵入性TVS-ET及宮腔鏡檢查／子宮內膜活檢侵入性評估之間的選擇，以分析其接受TVS-ET在子宮內膜癌的最低檢出率。

結果：200名女性完成調查。患者接受TVS-ET在子宮內膜癌的最低檢出率中位數為95%（四分位距80%-99.9%）。其中77名女性（38.5%）要求TVS-ET具有99.9%子宮內膜癌檢出率，才會考慮單以TVS-ET作為檢查方案。調查中發現曾經接受宮腔鏡檢查是唯一反映顯著性差異的因素：該組患者接受TVS-ET的檢出率顯著高於沒有宮腔鏡檢查經驗的患者（P=0.047）。

結論：調查中大部分女性接受單以TVS-ET檢查絕經後出血。臨床醫生應考慮患者的選擇、風險和接受程度，使患者能夠就絕經後出血的檢查做出妥善的知情選擇。

Introduction

Endometrial cancer is among the most common gynaecological malignancies worldwide. Among women with endometrial cancer, 90% initially report postmenopausal bleeding (PMB).[1-5] Approximately 10% of postmenopausal women are estimated to experience PMB.[1] Generally, there is no harmful underlying cause of PMB; however, women with recurrent PMB require medical assessment to distinguish between benign aetiology (eg, vaginal atrophy, uterine fibroids, and polyps) and endometrial cancer. Endometrial assessment is needed to exclude underlying malignancy.[2,6-10]

The endometrium can be examined non-invasively, using transvaginal sonography (TVS) to measure endometrial thickness (TVS-ET); alternatively, it can be examined invasively via blinded undirected endometrial sampling, saline infusion sonography, or diagnostic hysteroscopy.[11-13] Although both TVS-ET and blinded endometrial sampling are recommended as first-line investigations,[2,6,7,14-18] the gold standard approach for PMB investigation remains diagnostic hysteroscopy with visually guided endometrial sampling; this allows direct visualisation of the uterine cavity and histological investigation.[19]

Importantly, hysteroscopy is invasive and carries risks of complications such as infection, bleeding, uterine perforation, and visceral injury to the cervix or nearby organs (eg, bladder and bowel); it cannot be performed in women with cervical stenosis.[20] Additionally, some women report that hysteroscopy is uncomfortable and painful within an out-patient or office setting; thus, hysteroscopy, cervical dilation, and uterine curettage have been performed under general anaesthesia in such cases. Although TVS-ET has become an established investigational tool, there remains a lack of consensus concerning the endometrial thickness (3, 4, or 5 mm) that constitutes 'abnormal'. Our previous study of 4300 women with PMB demonstrated that 3% of women with PMB and endometrial thickness ≤3 mm had endometrial cancer.[21]

Patient preference regarding investigation approach is an important component of the decision care pathway. Individual women must balance the risks associated with an invasive procedure (eg, diagnostic hysteroscopy) with the risk of missing an endometrial cancer diagnosis if they select a non-invasive assessment (eg, TVS-ET). To our knowledge, the nature of this balance has not been assessed. The aim of the present study was to determine the extent to which women with PMB would accept the risk of missing endometrial cancer if they were to undergo TVS-ET as the first investigation of PMB.

Methods

This cross-sectional study was conducted in a tertiary centre in Hong Kong from June 2016 to June 2017. Women referred by either primary or secondary healthcare providers to the One-stop PMB Clinic for assessment and management were invited to participate in the study. Patient assessments included history taking, physical examination, pelvic ultrasound to measure endometrial thickness and screen for other pelvic pathologies, Pap smear (for women without recent Pap smear records), endometrial sampling with or without hysteroscopy. Women were excluded if they had <1 year of amenorrhea; had a prior TVS finding of endometrium thickness ≥5 mm; were aged ≥70 years; had dementia or mental retardation; and/or were unable to read or understand Chinese.

Prior to their clinic consultation, study participants completed a structured interview that was administered by an independent interviewer. Women were asked to first read an information leaflet regarding PMB, which described the risk of endometrial cancer, possible investigation options, and the risks associated with each option. The leaflet and interviewer explained that hysteroscopy and endometrial biopsy were expected to achieve a 100% detection rate, but these methods involved risks of pain, bleeding, infection, and uterine perforation related to uterine cavity exploration. The leaflet and interviewer also explained that TVS-ET did not

require entry into uterine cavity but would potentially miss some cases of endometrial cancer. The leaflet and interviewer did not disclose the percentage of endometrial cancers that would fail to be detected by TVS-ET. After they had read the leaflet, women were asked to complete a study questionnaire regarding their sociodemographic characteristics and their personal and family histories of gynaecological cancer; they also completed the Chinese version of the 20-item State-Trait Anxiety Inventory to measure their trait and state anxiety levels. The women's state and trait scores were categorised as above or below the scale midpoint. Women then underwent assessment of utilities regarding examination by either hysteroscopy or TVS-ET and the possibility of a missed cancer diagnosis, using the standard gamble technique.[22]

The standard gamble technique is the gold standard method used to determine utility towards a particular health state when a risk is involved. Individuals are asked to choose whether they prefer to have a certain guaranteed option or health state with a guaranteed outcome and no risk, or whether they would prefer an alternative option which entails some risk. The risks for the two health states are varied until the individual becomes indifferent to either option. At the point of indifference, the 'utility' for the health state under consideration is considered equal to 'p', while the utility of the alternative health state is considered equal to '1–p'.

Women were first asked to complete a standard gamble related to blindness, thereby ensuring that they understood the process. Subsequently, they were asked to complete a standard gamble to test their preferences towards the investigations of PMB. Each woman was asked to choose between the following tests: (1) TVS-ET, which is less invasive but involves some risk of missing endometrial cancer (probability of 1–p), or (2) an invasive test with hysteroscopy and endometrial biopsy, which detects 100% of all cancers but carries the risks described during the structured interview. To determine the level of acceptance of missing endometrial cancer during TVS-ET, the women were initially informed that the assumed detection rate of the TVS-ET was 75%; this detection rate was then increased in 5% intervals to 90%, then in 1% intervals to 98%, and finally in 0.1% intervals to 99.9%. We recorded the stated detection rate at which the woman was indifferent to either option. The missed endometrial cancer rate that women would accept to avoid an invasive procedure was defined as 1–detection rate.

Sociodemographic characteristics, past and current gynaecological history findings, and anxiety levels are presented as mean ± standard deviation or median and interquartile range; qualitative variables are presented as absolute frequency and percentage. The acceptable rate of endometrial cancer detection by TVS-ET alone, as an alternative to invasive hysteroscopy/biopsy, is presented as median and interquartile range. Differences in scores among sociodemographic groups were compared using the Mann-Whitney *U* test. SPSS software (Windows version 20; IBM Corp, Armonk [NY], United States) was used for all statistical analyses. A P value of <0.05 was considered statistically significant.

Results

During the study period, 202 women agreed to participate in the study; 200 of these women completed the questionnaires and the standard gamble assessments. Table 1 summarises the sociodemographic, obstetric and gynaecological histories, and anxiety levels of these 200 women. Overall, 11 (5.5%) of the 200 women were subsequently diagnosed with cancer or an atypical endometrium: nine had endometrial cancer, one had cervical cancer, and one had atypical hyperplasia. Among 42 patients who underwent Pap smears in our clinic, smear results showed atypical glandular cells in two patients with endometrial cancer, while four patients with endometrial cancer had a shift in vaginal flora suggestive of bacterial vaginosis; the remaining smear results were normal.

The median endometrial cancer detection rate or utility that women would require for selection of TVS-ET to avoid invasive hysteroscopy examination was 95% (interquartile range=80%-99.9%). Overall, 77 (38.5%) women required TVS-ET to have a 99.9% detection rate for endometrial cancer. Thus, 38.5% of the women in our cohort would require TVS-ET to be comparable with diagnostic hysteroscopy before they would accept TVS-ET as the sole method for examination of the endometrium and uterine cavity.

Table 2 summarises the results of univariate analysis of the relationships between patient characteristics and the TVS-ET endometrial cancer detection rate. Women with previous hysteroscopy experience required the endometrial detection rate by TVS-ET to be significantly higher than did women without previous hysteroscopy experience (P=0.047). There were no significant differences in required endometrial cancer detection rates by TVS-ET among other sociodemographic characteristics, past and current obstetric and gynaecological histories, and state or trait anxiety (Table 2).

Discussion

To our knowledge, this study is the first to utilise the standard gamble technique to evaluate patient preference with regard to approaches used for the investigation of PMB. Specifically, we assessed the extent to which women would prefer to avoid an invasive investigation (eg, hysteroscopy and biopsy) if a non-invasive alternative were available. Our

TABLE 1. Demographic characteristics of the study participants (n=200)*

Characteristics	
Age, y	55.7 ± 4.0
Parity	
Nulliparous	16 (8%)
Multiparous	184 (92%)
Age at menopause, y	51.3 ± 3.2
Body mass index, kg/m^2	24.7 ± 4.3
Marital status	
Single	12 (6%)
Married	170 (85%)
Divorced	16 (8%)
Widowed	2 (1%)
Education level	
Primary	68 (34%)
Secondary	108 (54%)
Tertiary	24 (12%)
Residence	
With family	188 (94%)
Alone	12 (6%)
Amount of bleeding	
Spotting/light/moderate	147 (73.5%)
Heavy	53 (26.5%)
Episodes of bleeding	
Single	103 (51.5%)
Multiple	97 (48.5%)
Personal history of cancer	9 (5%)
Family history of gynaecological cancer	28 (14%)
Friends with history of gynaecological cancer	94 (47%)
Family income, HK$/mo	
<10 000	40 (20%)
10 001-20 000	54 (27%)
20 001-30 000	42 (21%)
30 001-40 000	34 (17%)
>40 000	30 (15%)
Prior hysteroscopy experience	23 (12%)
Prior transvaginal ultrasound experience	95 (48%)
Prior endometrial sampling experience	32 (16%)
State-Trait Anxiety Inventory–State score	
<40	89 (44.5%)
≥40	111 (55.5%)
State-Trait Anxiety Inventory–Trait score	
<40	124 (62%)
≥40	76 (38%)

* Data are shown as No. (%) or mean ± standard deviation

findings suggested that TVS-ET would need to detect approximately 95% of endometrial cancers (or miss approximately 5% of endometrial cancers) for women to select TVS-ET with the intention of avoiding an invasive investigation. However, our analysis also suggested that nearly 40% of the participants required TVS-ET to detect nearly all endometrial cancers before they would select TVS-ET as the sole investigational approach.

There are sparse published data concerning patient preferences for the investigation of PMB. Our literature review revealed a single study by Timmermans et al.[23] However, that study was limited to 39 participants and the results were obtained via telephone survey. In contrast to our protocol, Timmermans et al[23] only assessed patient preferences after the women's investigations had been completed; thus, their reported clinical experiences and preferences might have been biased. In the present study, we adopted the standard gambling approach which enabled a more quantitative analysis of patient willingness to select a different investigational approach. The standard gamble method is the gold standard approach for assessment of preferences in an uncertain situation[24]; it can be used to express the outcomes of different choices. It has been used previously to explore the acceptable risk of miscarriage after a high-risk Down syndrome screening test[25-28]; it has also been used to explore patient preferences concerning the risks of other medical treatments.

Currently, endometrial thickness cut-off values in endometrial pathology or cancer screening differ among hospitals.[2,6,19] The most commonly used cut-off endometrial thickness value is 4 mm[2]. Our study population of postmenopausal women accepted an endometrial cancer detection rate of 95% when using TVS-ET alone, with the intention of avoiding the more invasive procedure of hysteroscopy/endometrial biopsy. In our previous study, TVS-ET offered endometrial cancer detection rates of 97%, 94.1%, and 93.5% using 3 mm, 4 mm, and 5 mm as respective cut-off values.[21] Thus, a TVS-ET cut-off of 3 mm would generally be consistent with the endometrial cancer detection accuracy that women in our study required for TVS-ET to be used as the sole investigational approach. In our study population, women with previous hysteroscopy experience required TVS-ET to have higher detection rates; hence, they preferred hysteroscopic assessment.

There were some limitations in our study. First, women aged ≥70 years were excluded because we presumed that they would have difficulty understanding the standard gamble technique and/or completing the study questionnaires without assistance. Second, although our sample size was sufficient to assess our primary goal, it was

TABLE 2. Univariate analysis of relationship between patient characteristics and acceptable endometrial cancer detection rate*

Characteristic	No. of patients (n=200)	Acceptable detection rate	P value
Age, y			0.757
≤60	173	95.0% (80.0%-99.9%)	
>60	27	90.0% (80.0%-99.9%)	
Parity			0.099
Nulliparous	16	82.5% (75.0%-99.7%)	
Multiparous	184	95.0% (80.0%-99.9%)	
Virgin			0.502
Yes	7	90.0% (75.0%-99.9%)	
No	193	95.0% (80.0%-99.9%)	
Body mass index, kg/m^2			0.584
≤30	178	95.0% (80.0%-99.9%)	
>30	22	92.5% (83.8%-99.9%)	
Education level			0.574
<Secondary	68	95.0% (80.0%-99.9%)	
≥Secondary	132	95.0% (80.0%-99.9%)	
Education level			0.121
<Tertiary	176	95.0% (80.0%-99.9%)	
≥Tertiary	24	90.0% (75.0%-99.9%)	
Family income, HK$/mo			0.551
≤40 000	167	95.0% (80.0%-99.9%)	
>40 000	30	94.5% (80.0%-99.9%)	
Episode of postmenopausal bleeding			0.251
1	103	90.0% (80.0%-99.9%)	
>1	97	95.0% (82.5%-99.9%)	
Amount of bleeding			0.294
Heavy	53	95.0% (90.0%-99.9%)	
Less than heavy	147	95.0% (80.0%-99.9%)	
Personal history of cancer			0.177
No	191	95.0% (80.0%-99.9%)	
Yes	9	99.9% (90.0%-99.9%)	
Family history of gynaecological cancer			0.177
No	172	95.0% (80.0%-99.9%)	
Yes	28	97.5% (90.0%-99.9%)	
Friends with history of gynaecological cancer			0.321
No	106	95.0% (80.0%-99.9%)	
Yes	94	95.0% (85.0%-99.9%)	
Prior hysteroscopy experience			0.047
No	177	95.0% (80.0%-99.9%)	
Yes	23	99.9% (90.0%-99.9%)	
Prior transvaginal ultrasound experience			0.535
No	105	95.0% (80.0%-99.9%)	
Yes	95	94.0% (80.0%-99.9%)	
Prior endometrial sampling experience			0.510
No	168	95.0% (80.0%-99.9%)	
Yes	32	95.0% (80.0%-99.9%)	
State-Trait Anxiety Inventory–State Score			0.051
<40	89	97.0% (80.0%-99.9%)	
≥40	111	90.0% (80.0%-99.9%)	
State-Trait Anxiety Inventory–Trait Score			0.992
<40	124	95.0% (80.0%-99.9%)	
≥40	76	95.0% (80.0%-99.9%)	

* Data are shown as median (interquartile range), unless otherwise specified

inadequate for subgroup analysis. Larger studies are needed to explore the relationships of specific patient characteristics with the acceptable rate of endometrial cancer detection by TVS-ET alone, particularly in relation to factors such as personal history of cancer or precancerous conditions. Finally, our findings concerning the acceptable rate of endometrial cancer detection by TVS-ET reflect the preferences of women who participated in our study; they may not be generalisable to populations with different sociodemographic characteristics or clinical management pathways.

Conclusions

Clinicians should incorporate patient preferences concerning the investigation of PMB to enable an informed choice about invasive testing to exclude endometrial cancer. Our study population accepted an endometrial cancer detection rate of 95% by TVS-ET alone; this rate could be used to guide the design of future PMB investigation strategies.

Author contributions

Concept or design: LWY Fung, ECW Cheung, ASW Wong, DS Sahota.
Acquisition of data: LWY Fung, ECW Cheung, ASW Wong, DS Sahota.
Analysis or interpretation of data: LWY Fung, DS Sahota.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

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Ethics approval

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