



The Evaluation of Endometrial Sampler SAP-1 in Screening Patients With General Risk of Endometrial Cancer: A Diagnostic Test Study

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Abstract

Objectives: In recent years, early screening for endometrial cancer (EC) has received increasing attention. EC screening is recommended to be conducted among high-risk and risk-increasing populations, while the general-risk population, even with symptoms, is not within the scope of screening. This study aims to explore the role of endometrial sampler SAP-1 as a sample-collecting tool to screen EC among patients with general risk.

Materials and Methods: From August 2018 to June 2023, 275 patients, who were hospitalized for undergoing hysteroscopy and were confirmed as having a general risk of EC, were enrolled in this retrospective study. Before the procedure, endometrial samples were firstly collected by the method of SAP-1, and then hysteroscopy curettage or electrotomy was conducted to gather endometrial samples. With the pathological results of the latter as the gold standard, the diagnostic efficacy of SAP-1 sampling was analyzed.

Results: The sample satisfaction rate of SAP-1 was 91.4%, slightly lower than that by method of hysteroscopy (95.1%), but there was no significant difference between the two methods ($P > 0.05$). The samples of 275 cases were satisfied with both methods. One case of endometrial carcinoma and one case of precancerous lesion were misdiagnosed as normal endometrium with SAP-1 sampling. The sensitivity, specificity and accuracy of SAP-1 in diagnosing endometrial carcinoma and precancerous lesions were 88.2%, 100% and 99.3%, respectively.

Conclusions: Applying endometrial sampler SAP-1 to screen EC among women with general risk of EC has high diagnostic efficiency, easy manipulation, high safety, and can be completed in outpatient service with outstanding cost-effectiveness, which as well is worthy of clinical promotion.

Keywords: Endometrial sampler, Endometrial cancer, Screen, General risk

Introduction

In recent years, with the gradual maturity and widespread application of screening technology, as well as the universal recognition of the preventive effect of HPV vaccine and timely intervention for precancerous lesions, the incidence of cervical cancer has slowed down or even shown a downward trend in developed countries such as Europe and America, and some cities in China. At the same time, the morbidity of endometrial cancer (EC) is rising year by year, and showing a younger trend (1). Given its anatomical and biological behavior characteristics similar to cervical cancer, as well as the successful experience in cervical cancer screening, early screening for EC has received increasing attention from scholars all over the world (2). It has been demonstrated that some excess estrogen status such as unopposed estrogen therapy, tamoxifen treatment, obesity, infertility, irregular menses etc, are high risk factors for developing EC (RR: relative risk 1.5-20) (3-6). According to the consensus of Chinese experts, EC screening is recommended to be conducted among high-risk and risk-increasing populations, while

the general-risk population, even with symptoms, is not within the scope of screening. Obtaining microscale endometrial tissue for pathological examination through endometrial biopsy by method of circular sampling device (SAP-1, shown in Figure 1) is an effective way for EC screening and early diagnosis (7). Although the prevalence of EC in the general-risk population is far lower than that in the high-risk and risk-increasing population, once missed diagnosis happens, it will be detrimental to the patient's psychology and physiological well-being, and even impact the prognosis. This study aims to explore the role of endometrial sampler SAP-1 in screening patients with general risk of EC.

Methods

Subjects

This retrospective study was performed in the Gynecology and Obstetrics Department of Macau Kiangwu Hospital. From August 2018 to June 2023, patients, who were hospitalized and planned to undergo hysteroscopy, were enrolled in this study. All of them had indications for

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Key Messages

- ▶ Endometrial sampler SAP-1 is a cost-effective tool to screen endometrial cancer among women with general risk, and worthy of clinical promotion.

hysteroscopy, including abnormal uterine bleeding and/or abnormal echo images in the uterine cavity indicated by ultrasound, and had no operation contraindications. Exclusion criteria: patients with at least one of the following conditions are considered as high-risk or risk-increasing population according to “Advices on standards of EC screening” issued in 2020 (7): (a) obesity, body mass index (BMI) ≥ 30 kg/m²; (b) Polycystic ovary syndrome; (c) No history of estrogen use without progesterone; (d) Late menopause age (>55 years old); (e) No childbirth history or primary infertility; (f) Long term treatment with tamoxifen (especially for patients over 50 years old or continuous tamoxifen treatment after menopause); (g) Age ≥ 45 years old with diabetes; (h) Lynch syndrome patients; (i) Those who have third-degree relatives with Lynch syndrome and have not performed relevant genetic testing; (l) Individuals with a family history of EC or colon cancer. All enrolled patients signed an informed consent form individually, and this study was approved by the ethics committee of our hospital.

Endometrial Sampling Methods

Under intravenous anesthesia in operation room, surgical procedure steps were all performed by the same experienced gynecologist and as follows: (a) Use endometrial sampler SAP-1, manufactured by Saipu Jiuzhou Company, Beijing, China, to perform microscale endometrial sampling. The method of application can refer to our previous research report (8); (b) Undergo hysteroscopy routinely; (c) Perform diagnostic curettage or hysteroscopic electric resection, and collect endometrial specimens; (d) The specimens were sent to the Pathology Department, fixed with 10% Formaldehyde solution, embedded in paraffin, and stained with hematoxylin-eosin (HE).

Histological Diagnosis Criteria

The pathological diagnosis of endometrial tissue refers to the WHO 2014 diagnostic criteria (9): normal endometrium (menopausal endometrium, proliferative endometrium, secretory endometrium, etc); Benign endometrial lesions (endometrial polyps, endometritis, endometrial hyperplasia without atypical hyperplasia, submucosal uterine fibroids, etc); Pre-cancerous lesions (atypical hyperplasia); Malignant lesions (EC, etc).

Evaluation Indicators

Satisfaction with pathological specimens: (a) Satisfactory: Sufficient endometrial specimens, visible glandular/interstitial ratio and glandular structure under microscope,

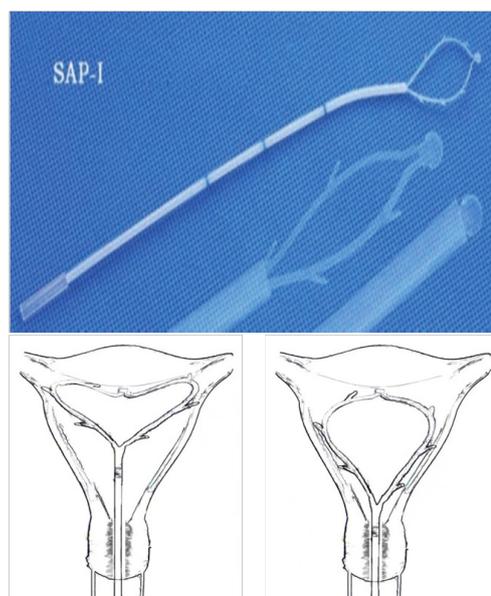


Figure 1. The SAP-1 Sampler Device. Reprinted with permission from Yu et al (8).

and able to make pathological diagnosis; (b) Dissatisfied: The amount of endometrial specimens is too small, and the tissue structure is discontinuous and fragmented, making it impossible to make a pathological diagnosis under the microscope.

Diagnostic efficacy: The sensitivity, specificity, misdiagnosis rate, missed diagnosis rate, and accuracy of SAP-1 sampling and hysteroscopic sampling for diagnosing EC.

Statistical Analysis

This study used SPSS 19.0 software for statistical analysis, and the measurement data was expressed in terms of rates and analyzed by the Chi-square test, with $P < 0.05$ as the difference with statistical significance.

Results

A total of 305 patients were included in this study. The patients' age ranged from 23 to 74 years (mean 40.4 ± 8.6 years). The flowchart was presented in Figure 2.

SAP-1 and Hysteroscopy Sampling Situation

279 cases were satisfied with SAP-1 sampling, while 26 cases were dissatisfied. The sampling satisfaction rate was 91.4%, slightly lower than 95.1% (290/305) of hysteroscopic curettage, but the difference was not statistically significant ($P > 0.05$), as shown in Table 1.

The Indexes of Efficacy of SAP-1 Sampling for Diagnosing EC and Precancerous Lesions

A total of 275 patients were satisfied with both SAP-1 and hysteroscopic sampling, and 17 patients with EC/precancerous lesions were diagnosed after hysteroscopic sampling. Among them, 1 patient with EC and 1 patient

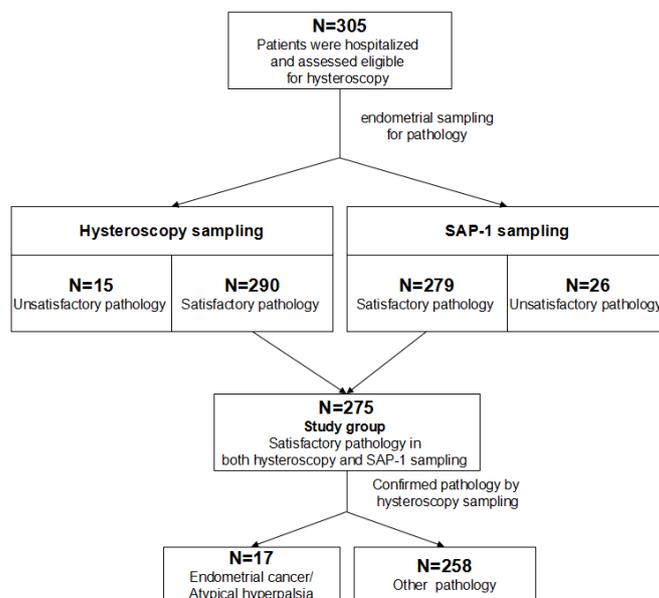


Figure 2. Flowchart of This Study.

with precancerous lesion was pathologically misdiagnosed as normal endometrium after SAP-1 sampling. According to statistics, compared with hysteroscopic sampling, the sensitivity, specificity, misdiagnosis rate, missed diagnosis rate, and accuracy of SAP-1 sampling for pathological diagnosis of EC and precancerous lesions are detailed in Table 2.

The Cost-Effectiveness of SAP-1 Sampling in Comparison to Hysteroscopy-Guided Sampling

The mean expenditure of SAP-1 sampling is much less than that of hysteroscopy guided curettage or hysteroscopic electric resection (1160 Macau dollars vs. 9180 Macau dollars, $P < 0.05$).

Discussion

In the past five years, academic organizations from different countries in the world have issued their own guidelines or consensus for EC screening, including Euro-American groups such as the American Cancer Society (10), the

International Federation of Gynecology and Obstetrics (FIGO) (11), the German Gynecological Oncology Group (AGO) (12), and the British Gynecological Oncology Society (BGCS) (13), as well as some Asian neighbors such as Japan (14) and South Korea (15). In 2020, a consensus document, on the basis of the diagnosis and treatment experience and screening status of EC in China, was issued by Chinese Obstetricians and Gynecologists Association. Based on different guidelines above, the following views are currently widely recognized: (a) The efficacy of EC screening among general-risk population still needs to be fully confirmed, and is not considered as a routine recommendation. Screening is only recommended for high-risk or risk-increasing populations; (b) Trans-vaginal ultrasound (TVU), as an optional screening method, has high sensitivity but low specificity, low positive predictive value and high false positive rate, and there are inevitable operator- and instrument-related errors. TVU is not recommended as a separate screening method, but only for preliminary evaluation; (c) Currently, there is no

Table 1. Comparison of Satisfactory Rate Between Two Sampling Methods

Sampling Methods	Satisfactory (n)	Unsatisfactory (n)	Satisfactory Rate (%)	χ^2	P
SAP-1	279	26	91.4	3.16	0.075
Hysteroscopy	290	15	95.1		

Table 2. Efficacy of SAP-1 Sampling for Diagnosing Endometrial Cancer and Precancerous Lesions

Hysteroscopy	EC and Precancerous Lesion		Sensitivity % (95% CI)	Specificity % (95% CI)	Mis-diagnosis Rate (%)	Missed Diagnosis Rate (%)	Accuracy % (95% CI)
	SAP-1 +	SAP-1 -					
+	15	2	88.2 (62.3-97.9)	100 (98.2-100)	0	0.77	99.3 (96.9-99.9)
-	0	258					

identified and unified screening method for EC. Most guidelines recommend the application of outpatient disposable endometrial samplers, represented by Pipelle and Tao brush, to obtain endometrial specimens by method of negative pressure suction or circular scraping for cytological or micro-histopathological diagnosis.

It cannot be denied that diagnostic curettage, or assisted by hysteroscopy, is still the gold standard method for the diagnosis of EC. However, the procedure, requiring high techniques and carrying the risk of complications such as uterine perforation, infection, and anesthesia accidents, is not suitable for routine and commonly-conducted screening processes. Previous studies have shown that the efficacy (positive and negative predictive values) of simple screening devices such as Pipelle and Tao brush for diagnosing EC is not inferior to hysteroscopy-assisted curettage (16). Currently, this sampling way has become a new, simple, safe, painless, and cost-effective screening method. Endometrial sampler SAP-1 was invented by Chinese scholars and has been used in clinical screening practice by many Chinese medical institutions. Our research team has recently used SAP-1 to screen EC among postmenopausal women (2). As well as the current results of this study, the sample satisfaction rate and diagnostic coincidence rate of SAP-1 sampling are ideally more than 90%, consistent with the literature reports (17,18), and similar to other types of endometrial sampling devices (19). And this method has been widely recognized by Chinese experts (7). Naturally, most ECs evolve relatively slowly, and most EC patients are diagnosed in the early stage. In addition, there is currently no identified and efficient screening method, so most guidelines did not routinely recommend EC screening among general-risk population. However, in recent years, the prevalence of EC has shown a rising and younger trend, and there are many patients latent in general-risk population. Especially those, who complain of abnormal bleeding and other symptoms or ultrasound indicating abnormal intrauterine images, will not have a peace mind. Therefore, this study attempted to explore among patients in this condition, and the results showed that taking pathological results of endometrium sampled by hysteroscopy as the gold standard, the sensitivity, specificity, and accuracy of SAP-1 sampling in diagnosing EC and precancerous lesions were 88.2%, 100%, and 99.3%, respectively. Among them, one patient with EC and one patient with precancerous lesion missed diagnosis, and the pathology showed that focal lesions were detected in both patients. The lesions were located in the local part of the proliferating endometrium and the local part of endometrial polyp respectively, and the missed diagnosis may originate from the fact that SAP-1, as an EC screening tool, is unable to completely cover all the endometrium in the uterine cavity, so there is a certain chance of missed curettage. In addition, SAP-1 can only gather mucosal tissue on the surface of the uterine cavity, but cannot obtain interstitial or muscular tissue below

it. Therefore, SAP-1 is not fit for specimen collection of intrauterine occupying lesions such as fibroids and polyps (8,17,20,21). Moreover, three other EC-suspected patients in our research team were diagnosed by SAP-1 sampling successfully in the outpatient department without anesthesia or cervical dilation, and following confirmation by hysteroscopy.

The present study has certain limitations that should be noted. First, the pain during the endometrial sampling process cannot be evaluated under anesthesia status. Second, for some patients, the sample amount of SAP-1 method is quite less, which will lead to the difficulty in judgement for pathologist. Therefore, the application of SAP-1 in EC screening among general-risk population still needs further study to verify.

In summary, given the good diagnostic efficacy of SAP-1 and the low cost, the vast majority of operations do not require cervical dilation, are simple and easy to perform, do not require anesthesia, and have high safety. It can be performed in outpatient settings with outstanding cost-effectiveness. Therefore, screening for EC in the general risk population is also worthy of clinical promotion and SAP-1 could be considered as a simple and practical device for this process.

Authors' Contribution

HHY, ZW and LH contributed to conceptualization, design and methodology of the work. HY, LC, LH and CQ contributed to endometrium sampling, data curation and interpretation of data. HY, ZW and LH contributed to data formal analysis. HY was responsible for funding acquisition, overall supervision, project administration and contributed to interpretation of the results. LC, LH and CQ were in charge of resources, software, validation and visualization. HY, LC and LH drafted the manuscript, which was reviewed and edited by ZW and LH. All authors read and approved the final manuscript.

Conflict of Interests

The authors have no proprietary, financial, professional, or other personal interest of any nature in any product, service, or company.

Ethical Issues

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. Informed consent was obtained from all individual participants included in the study.

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