Endometrial Sampling for Endometrial Cancer: Still the Gold Standard?

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Endometrial Cancer (EC)

Is the most common gynaecological malignancy affecting women in developed countries and the second most common gynaecological malignancy world-wide, due to the higher rates of cervical cancer in the developing world [1]. The incidence of EC is steadily increasing, largely owing to an ageing population and escalating rates of obesity [2]. According to International Federation of Gynecology and Obstetrics (FIGO), EC is a major differential diagnosis of AUB in the reproductive women [3]. Despite the frequency of this disease, awareness amongst the general population is low and EC research is somewhat underfunded relative to its societal burden [4].

In the past, multiple attempts to evaluate the histological grade preoperatively were without significant success [5,6]. Dilatation and curettage (D&C) were once the gold standard for endometria sampling and routinely used with an upgrade rate of 17-26%, compared to the final pathology [7-9]. In an attempt to develop a less invasive diagnostic method, office endometrial sampling became progressively popular. However, studies aimed at investigating office biopsies revealed an apparent inaccuracy in histological grading with an upgrade rate of nearly 30-50%, compared to hysterectomy pathology [10]. Cotillo et al. [11] investigated the accuracy of transcervical resectoscope (TCR) and revealed a rather optimistic finding of 97.1% correlation with the final pathology.

This could be a solution to overcome the hurdle of inevitable upgrades. This method allows direct visualization, a targeted biopsy, and theoretically a more accurate evaluation of preoperative tumour grading [11]. There is also recent progress with effort at improving the diagnostic accuracy of endometrial cancer through immunohistochemistry biomarkers targeting endometrial hyperplasia and predicting progression of endometrial hyperplasia to endometrial cancer [12]. There is need for the clinician to consider therefore the possibility of ECs when treating an abnormal uterine bleeding.

Furthermore, we experienced a case scenario where a colleague had multiple endometrial sampling done and each sample sent to different pathologist and the outcome of the histopathology reports was bizarre. The results were that of different reports establishing the inconsistencies associated with endometrial sampling for endometrial cancer. Similar, encounters have been reported in literature which is the bane of this editorial report. The great question we need an urgent answer for remains "is endometrial sampling for endometrial cancer still the gold standard?"

Abnormal Uterine Bleeding (AUB)

May be defined as any variation from the normal menstrual cycle related to reproductive status; as well as other bleeding not related to menses provides the terminology and descriptions are consistent with the FIGO Menstrual Disorders Working Group consensus statement [13,14]. AUB is the direct cause of a significant health care burden for women, their families, and society as a whole. Up to 30% of women will seek medical assistance for this problem during their reproductive years [15-17]. Patients with AUB are at risk for endometrial carcinoma and therefore AUB warrants further investigation [18]. Histological endometrial assessment is indicated when a patient presents with AUB and an increased endometrial thickness on transvaginal sonography (TVS) [19,20]. Outpatient endometrial biopsy is the least invasive technique to obtain tissue for histological assessment. Endometrial biopsies have a very high sensitivity for diagnosing an endometrial (pre)malignancy in AUB women (95%) [21].

Furthermore, performing an endometrial biopsy in women with AUB with increased endometrial thickness is the most cost-effective strategy [22]. Yet, 7-68% of outpatient endometrial biopsy samples are inconclusive because the amount of tissue obtained is insufficient for a reliable histopathological diagnosis [22-25]. In such cases, a more invasive hysteroscopy or dilatation and curettage (D&C) is necessary in order to rule out endometrial carcinoma or atypical hyperplasia, which is present in 6% of these women [23]. The high failure rate due to inconclusive endometrial biopsies might affect the cost-effectiveness of the diagnostic work-up.
Reports from the literature suggest that the attempts to increase the diagnostic efficiency of outpatient endometrial biopsy by structured assessment have not yielded significant improvement in outcome. Therefore, these women cannot be reassured without further invasive, diagnostics [23]. Reviewing hospital protocols revealed that standardized sampling methods was not available in most hospitals, let alone the recommendations on using a tenaculum, entering the uterine cavity more than once, or the use of analgesia in painful procedures. In the cost-effectiveness analysis by Clark et al, the failure rate due to inconclusive endometrial biopsy samples was 12% (95% CI 0.09-0.15) based on a systematic review [22,23]. Other studies reported a failure rate of 7-68% [22-25].

The Clinical Importance of a Diagnosis of Endometrial Hyperplasia (EH)

relates to the long-term risk of progression to endometrioid EC and it is generally accepted that cytological atypia is the principal histological characteristic when assessing EHs for malignant potential [26]. However, not all EHs will progress to malignancy; some EHs occur secondary to estrogenic proliferation without an underlying malignant mechanism. These patients may be asymptomatic and, in some cases, the EH may regress without ever being detected. Several histological classification methods have been proposed aiming to correlate EH architecture and cytological features with the risk of progression to endometrioid EC [27].

The two prominent classification systems are

a. The World Health Organization (WHO) system, established in 1994 with revision in 2003, which is widely known within current clinical gynaecological practice and

b. The endometrial intraepithelial neoplasia (EIN) system, introduced in 2000 [28] and was endorsed in 2014 by the WHO as part of their most recent classification of tumours of the female reproductive organs [29].

The Endometrial Intraepithelial Neoplasia (EIN)

Classification system divides hyperplastic endometrial lesions into two groups:

a. Benign EH and

b. EIN. This is based on objective diagnostic criteria that can be determined from a haematoxylin and eosin (H&E) stained endometrial section.

These criteria emulate what the D-score achieves; however, they can be ascertained quickly by a pathologist using routine light microscopy [30]. EIN lesions are defined as mononuclear proliferations of architecturally and cytologically altered premalignant endometrial glands, which are prone to transformation to endometrioid EC [28].

Conclusion

It is mandatory for clinicians assessing AUB to recognize this disease entity as a possible differential diagnosis. Reports from literature corroborate the fact that there is a high risk of missed diagnosis with less invasive pre-operative diagnostic method of office endometrial trial sampling. The new progress in search of immunohistochemical biomarkers may eventually lay to rest the inconsistent histopathology reports for endometrial biopsy in the nearest future.

References


