THE ROLE OF ENDOMETRIAL VOLUME IN THE PREDICTION OF ENDOMETRIAL HYPERPLASIA

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- **2D/US:** Two dimensional ultrasonography
- **3D/US:** Three dimensional ultrasonography
- **ASUMH:** Ain Shams University Maternity Hospital
- **AUB**: Abnormal uterine bleeding
- **AP 1:** activator protein 1
- **D&C:** Dilatation &Curettage
- **DUB:** DYSFUNCTIONAL UTERINE BLEEDING
- **EIC:** Endometrial intraepithelial carcinoma
- **EIN:** Endometrial intraepithelial neoplasia
- **EMP**: Endometrial polyp
- **HPV:** human papilloma virus
- **IGF1R**: insulin-like growth factor 1 receptor
- **L.M.P:** last menstrual period
- **ROI:** Region of interest
- **TAU:** Trans-abdominal Ultrasonography
- **TVU:** Trans-vaginal ultrasonography
- **UPSC:** Uterine papillary serous carcinoma
- **UKCTOCS**: UK collaborative trial of ovarian cancer screening
- **VOCAL:** Virtual Organ Computer-aided AnaLysis
- **VPS :** Volume percentage stroma

Protocol

Pre menopause is a transitional time 3-5 years prior to menopause that is usually characterized by a change in the normal menstrual cycle. The cycles may be shorter or longer, and the flow may vary from light to heavy. As ovarian function is declining, ovulation may not occur. The estrogen that has been released will cause the uterine lining to thicken. Without progesterone to oppose the estrogen, the lining will continue to build-up; and breakthrough bleeding can result **(Fallowfield L et al.,2011).** This abnormal, thickening of the endometrium is called hyperplasia, and in some instances, it may ultimately lead to endometrial cancer. Polyps and fibroids, which are benign, may also cause changes in bleeding pattern **(Nandi and Poretsky,2013).**

Pre menopause is defined as the period surrounding th menopause (before, during and after). The length of this period varies, but it is usually considered to last approximately 7 years, beginning with decline in ovarian function in a woman's40s and continuing until she has not had a menstrual period for 1 year **(William et al., 2007).**

Endometrial hyperplasia is defined as an increased ratio of endometrial glands to stroma greater than one to one **(Hannemann et al., 2007).** Some have suggested that the term endometrial hyperplasia should be used to describe lesions without atypia and prefer the term endometrial intraepithelial neoplasia to describe lesions that exhibit nuclear atypia **(Speroffand Fritz, 2005).** In the current WHO classification, these types of hyperplasia are further subdivided into those with typical or atypical cytology **(Ferri, 2011).**

Endometrial hyperplasia peak incidence from 1985–2003, Group Health, Seattle, Washington was: simple, 142 per 100,000 woman-years, complex, 213 per 100,000 woman-years, both in the early

50s; and atypical, 56 per 100,000 woman-years in the early 60s. Age-adjusted incidence decreased over the study period, especially for atypical hyperplasia **(Reed SD1 et al., 2009) .**

And The incidence of GCTs in the period 1991–2012 from the European Society of Gynecological Oncology Was: 0.61 per 100,000 women per year. Concurrent endometrial cancer at the time of diagnosis of GCT was found in 58 patients (5.9%) and endometrial hyperplasia in 251 patients (25.5%), including complex hyperplasia in 89 patients (9.1%) and simple hyperplasia in 162 patients (16.5%). Long-term follow-up of 490 patients (47.5%) without a hysterectomy showed that endometrial abnormalities were found in 10 patients (2.0%) of which 2 had endometrial cancer. Interestingly, 8 (80%) of the 10 patients with endometrial abnormalities had recurrent GCT at the time of diagnosis of endometrial hyperplasia or cancer **(Van Meurs et al., 2013).**

Several risk factors for the development of endometrial hyperplasia & cancer have been identified. Most of these risk factors are related to prolonged, unopposed estrogen stimulation of the endometrium. Nulliparous women have 2 to 3 times the risk of parous women. Infertility and a history of irregular menses as a result of anovulatory cycles increase the risk. Natural menopause occurring after age 52 years increases the risk for endometrial cancer 2.4 times compared with women who experienced menopause before 49 years of age, probably as a result of prolonged exposure of the uterus to progesterone-deficient menstrual cycles. The risk of endometrial cancer is increased 3 times in women who are 21 to 50 pounds overweight and 10 times in those more than 50 pounds overweight **(Lurain., 2007).**

Abnormal uterine bleeding is the cause of many gynecological visits in pre and postmenopausal and can be due to the presence of either benign conditions, e.g., leiomyoma (uterine fibroids), endometrial polyps, endometrial hyperplasia, and adenomyosis, or the presence of endometrial cancer**(Burbos et al., 2010).**

Endometrial sampling is the ‘‘gold standard’’ for diagnosing abnormalities in the endometrial tissue of patients with PMB especially for diagnosing diffused endometrial conditions such as endometrial cancer and endometrial hyperplasia **(Holalkereet al., 2009).**Since the sensitivity of endometrial sampling has been estimated to range from 85% to 95%, there has been a growing trend toward using a noninvasive procedure, such as high-resolution transvaginal sonography (TVS), to measure the endometrial thickness and to classify cases as being at low or high risk for malignancy, thus avoiding unnecessary sampling **(Dimitraki et al., 2010).**

Endometrial sampling is usually considered necessary only in women with premenopausal bleeding and endometrial thickness ≥5 mm**)** However, many women with premenopausal bleeding and endometrial thickness ≥5 mm do not have endometrial cancer and some do not have any endometrial pathology at all, but will still undergo – perhaps unnecessarily interventional diagnostic procedures such as dilatation and curettage (D&C) or hysteroscopy **(Opolskiene et al., 2009).**

D&C is seldom necessary to evaluate abnormal uterine bleeding and has significant surgical risks beyond general anesthesia **(Soguktas et al., 2012).** Complications may arise from either the introduction or spreading of infection, adverse reaction to general anesthesia required during the surgery or from instrumentation itself, if the procedure is performed blindly without the use of any imaging technique such as ultrasound or hysteroscopy. One risk of sharp curettage is uterine

perforation,cervical or uterine trauma that can occur with cervical dilation and instrumentation of the uterus **(Pazol.,2014).**

Hysteroscopy is a valid alternative to D&C for many surgical indications from diagnosis of uterine pathology to the removal of fibroids and even retained products of conception. It poses less risk because the doctor has a view inside the uterus during surgery, unlike with blind D&C **(Dimitraki et al., 2010).**

Transvaginal ultrasound (TVUS) is a method routinely used for differentiating between the causes dysfunctional uterine bleeding such as adenomyosis, endometrial polyps and leiomyomas. However, in TVUS images it is difficult to distinguish between a thickened endometrial lining and other diffuse or focal endometrial abnormalities ***(Goldstein, 2010).***

Trans-vaginal ultrasonography can reliably assess thickness and morphology of the endometrium and can thus identify a group of women with postmenopausal bleeding who have a thin endometrium and are therefore unlikely to have significant endometrial disease. This group may not require any further investigation unless there is a recurrence of the bleeding **(Moschos and Twickler, 2008).**

3D ultrasound tomography combines the advantages of ultrasound, e.g. safety ,simplicity of application and inexpensiveness (in contrast to MRI and CT), with the advantage of the third dimension. The process of constructing a 3D image out of 2Dsections is conventionally done by the brain of the investigator **(Belitsos et al., 2012).**

Another important ability of 3D US is volume calculation using the Virtual Organ Computer-aided AnaLysis (VOCAL™) even in irregularly shaped structures. This method has been demonstrated to be more accurate than 2D-volume estimation **(Alcazar and Galvan,2009).**

3D ultrasound imaging discriminate better between benign and malignant endometrium than do endometrial thickness measurements **(Yaman et al., 2008).**Three dimensional sonography allows simultaneous visualization of the three orthogonal planes along with the three dimensional rendering mode. Three dimensional rendering mode of the uterine cavity allows ruling out endometrial pathology with almost absolute certainty **(Katz, 2007).**

The only way to measure the endometrial volume is to outline its surface in a number of parallel sections, which would take into consideration irregularities of its shape. This is the principle of volume measurement used with three-dimensional ultrasound equipment **(Kupesic et al., 2000).**

Although the value of volume measurements, compared with that of endometrial thickness in differentiating between benign and malignant endometrial pathology. The differentiation between endometrial hyperplasia and cancer using 2D ultrasound was not possible due to overlap in the endometrial thickness measurements. When 3D volume measurements were performed, the overlap was much smaller which significantly improved the diagnosis of cancer.

Volume measurement showed significant differences in size between endometrial hyperplasia and polyps, which were not detected by the measurement of endometrial thickness. This may be explained by the fact that polyps are usually localized thickenings of the endometrium that do not affect the whole of the uterine cavity **(Timmermanset al.,2010).**

Three dimensional rendering did allow distinguishing with much more clarity between atrophic endometrium, polyps, focal and generalized hyperplasia and carcinomas. Polyps of just few millimeters in size could be observed with shape, size and precise location of the implantation base of the polyp **(Najeeb et al., 2010).**