Abnormal Uterine Bleeding

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The normal Uterine period

- Blood loss < 80 ml (average 30-35 ml)
- Duration of flow 2-7 days (average 4 days)
- Cycle length 21 - 35 days (average 28 days)

Phases of the menstrual cycle

- Follicular ◦ Begins with Menses ends with luteinizing (LH) hormone surge

- Ovulation (30-36 hours) ◦ Begins with LH surge and ends with ovulation

- Luteal (14 days) ◦ Begins with the end of the LH surge and ends with onset of menses

Abnormal uterine bleeding (AUB)

- Definition: Any change in menstrual period as regard:
- quantity
- Duration
- schedule

Why it is important

- Abnormal uterine bleeding affects 10 to 30 percent of reproductive-aged women and up to 50 percent of perimenopausal women
- It is a common reason for gynecologic consultation.
- Responsible for over one third of hysterectomies.

PALM-COEIN classification system for abnormal uterine bleeding in nongravid reproductive-age women

Polyp
Adenomyosis
Leiomyoma
Malignancy & hyperplasia

→

Submucosal
Other

Coagulopathy
Ovulatory dysfunction
Endometrial
Iatrogenic
Not yet classified

- P: Endometrial polyp IMB or PCB in 30-50 year old woman
- A: Adenomyosis – Dysmenorrhea, dyspareunia, chronic pelvic pain, sometimes menorrhagia
- L: Leiomyoma – Submucous myoma – Menorrhagia; rarely IMB; never metrorrhagia AUB: Structural Conditions

❖ M: Malignancy and hyperplasia

✓ Adenomatous hyperplasia (AH) -atypical AH-endometrial carcinoma

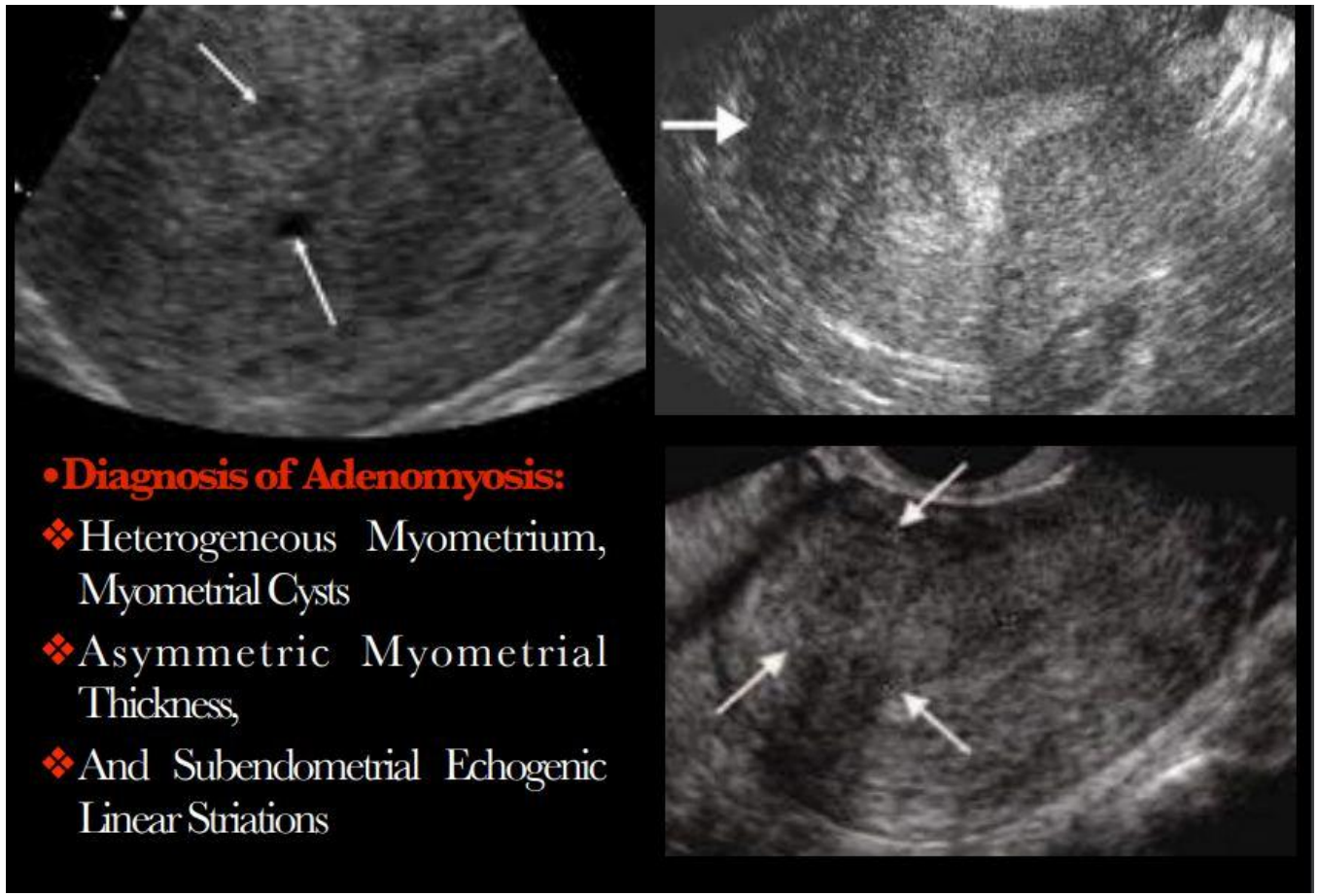
- Post-menopausal bleeding
- Recurrent perimenopausal metrorrhagia
- Chronic anovulator (PCOS) with metrorrhagia –

✓ Leiomyosarcoma •

Post-menopausal bleeding

Sonohysterography

Sonohysterography polyps

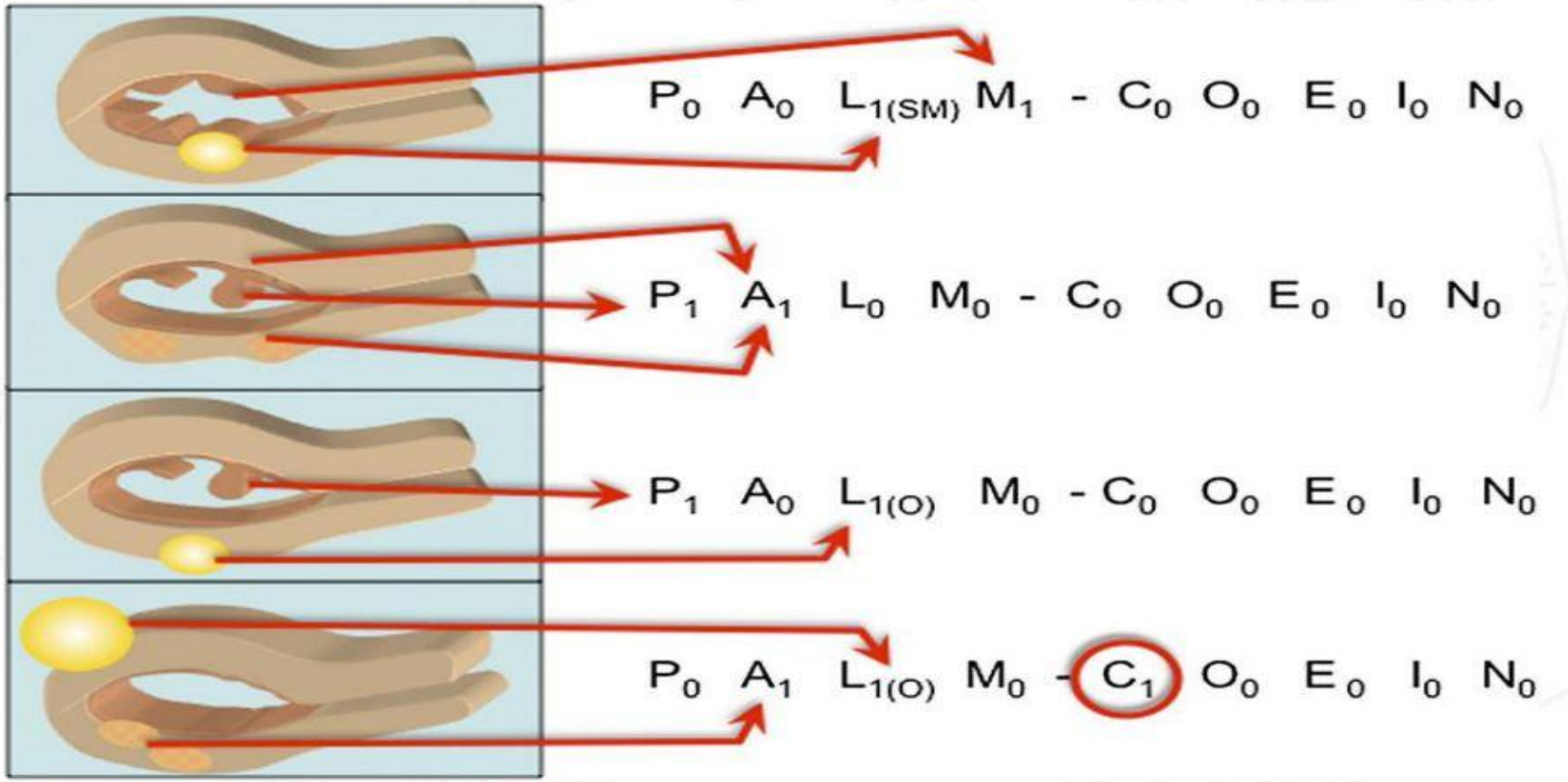

•Diagnosis of Adenomyosis:
❖Heterogeneous Myometrium, Myometrial Cysts
❖Asymmetric Myometrial Thickness,
❖And Subendometrial Echogenic Linear Striations

TV Ultrasound Vs. SIS

TV Sonography: Sensitivity 55-75% in exclusion of uterine & endometiral pathology

SIS Is Superior To TV US In Detection Of Intracavitary Lesions.

FIGO classification system for causes of abnormal uterine bleeding in the reproductive years



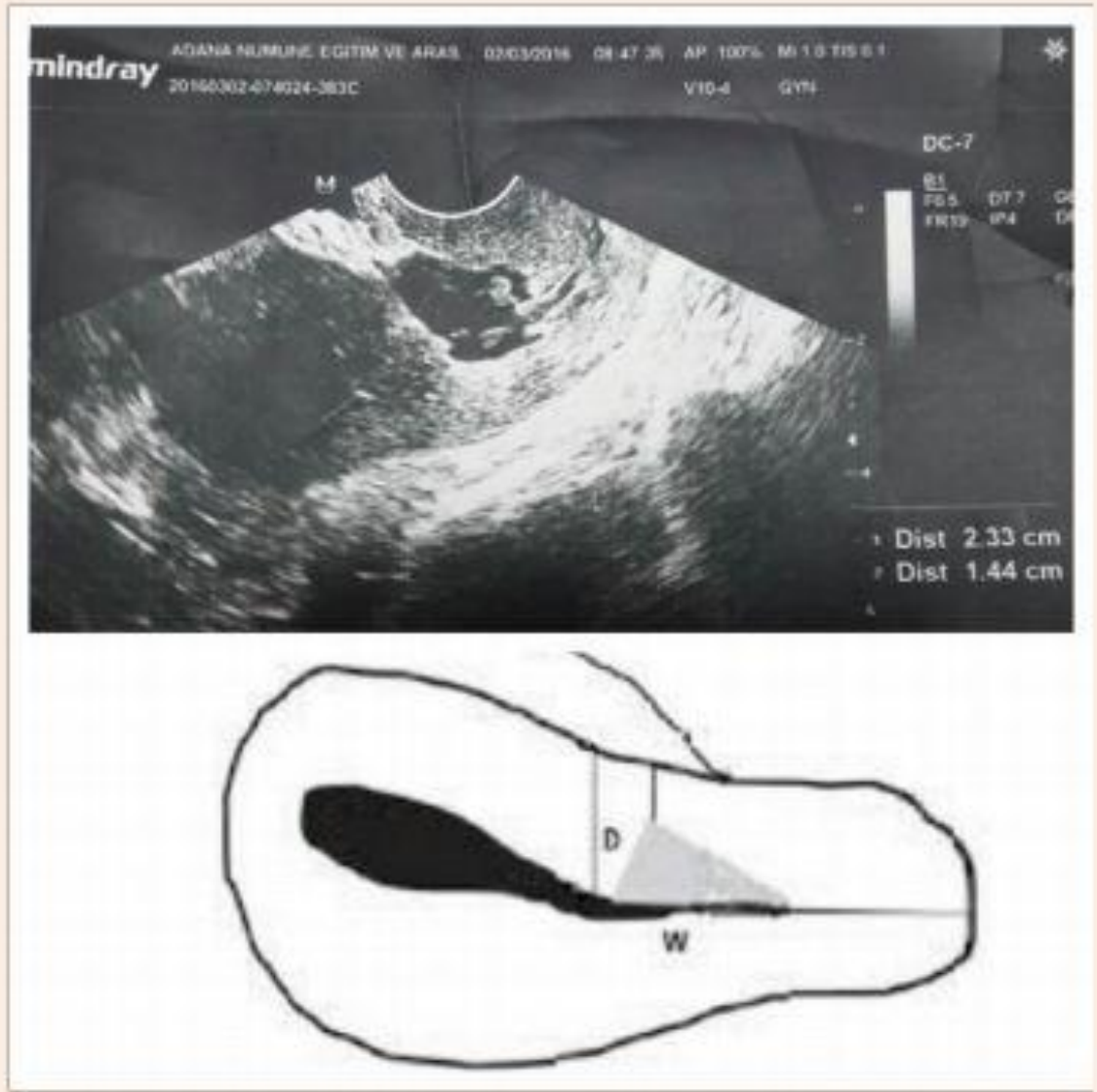
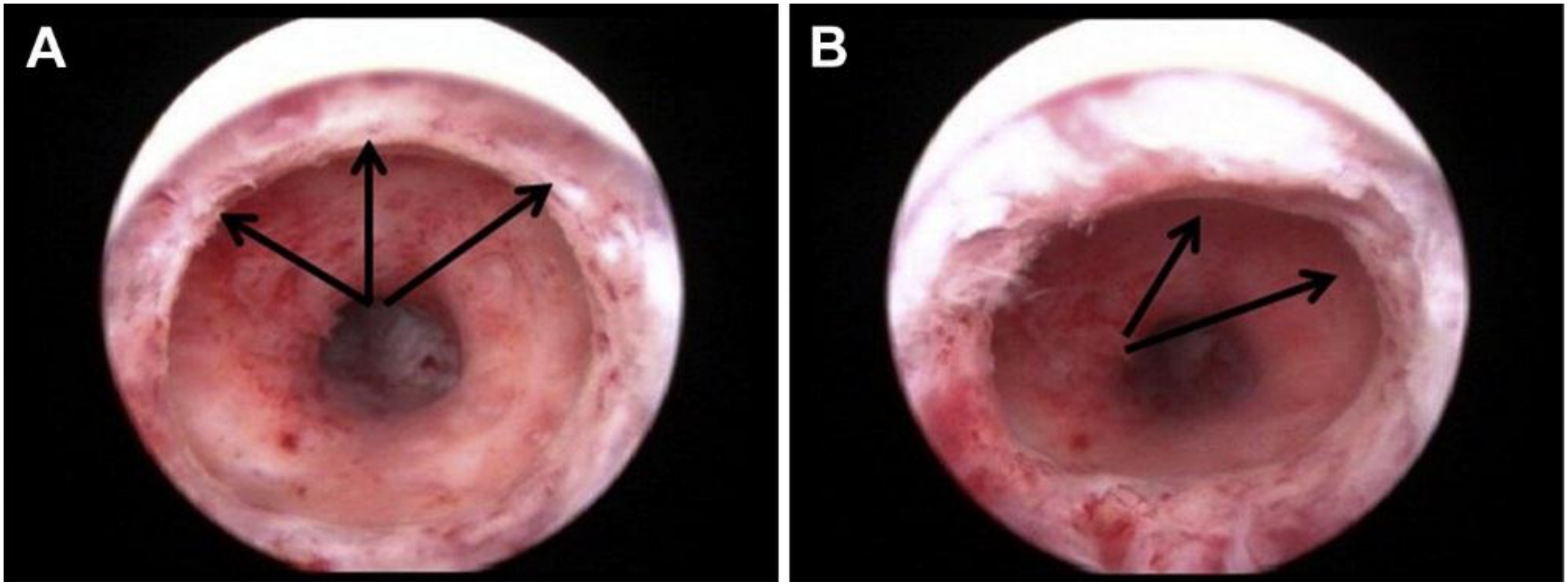
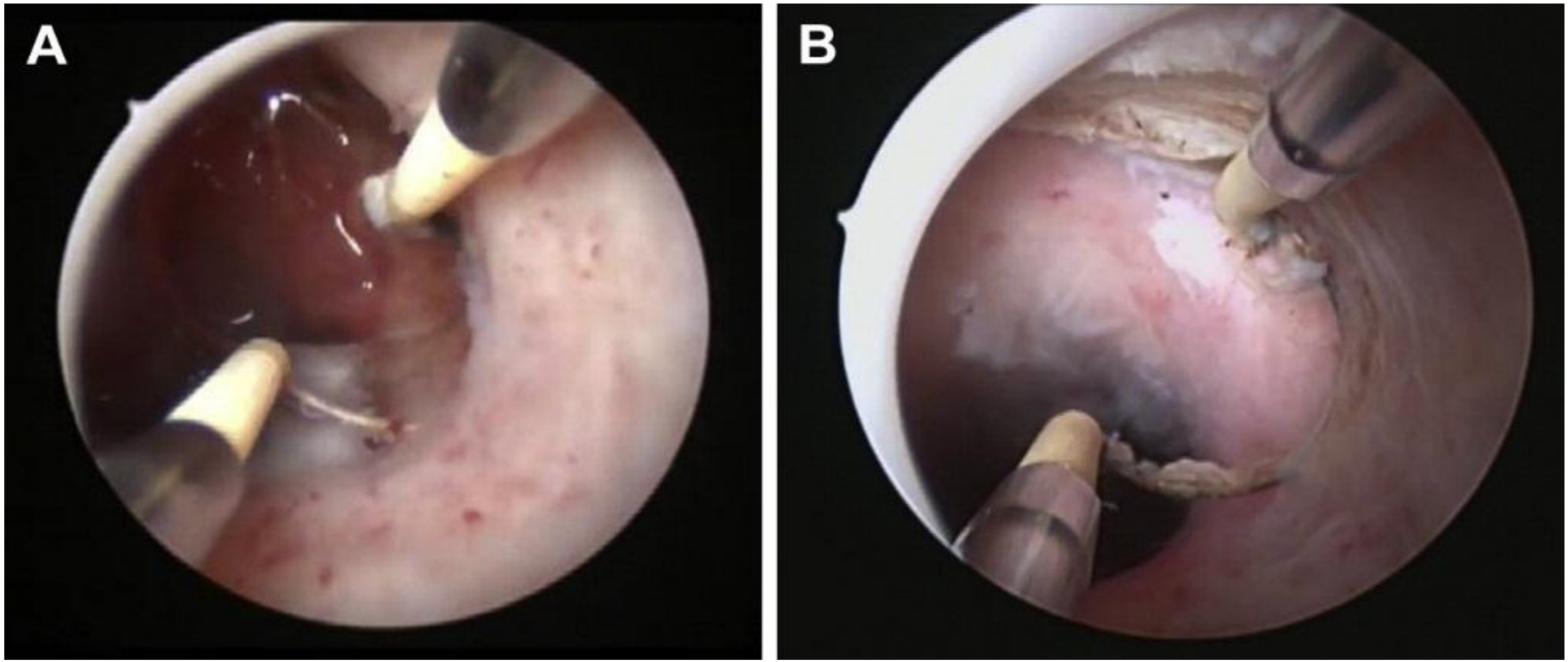


Figure 1: Ultrasonographic image and diagram of caesarean scar defect "isthmocele"


A
B


A
B

COEIN

- Clotting factor deficiency or defect

✓ Liver disease

✓– Congenital (Von Willebrands Disease)

- Platelet deficiency (thrombocytopenia) with platelet count <20000

✓Idiopathic thrombocytopenic purpura (ITP)

✓ Aplastic anemia

- Platelet function defects

❖Screen for underlying disorder of hemostasis if any of

- Heavy menstrual bleeding since menarche
- One of the following

✓ Post-partum hemorrhage
✓ Bleeding associated with surgery
✓ Bleeding associated with dental work

- Two or more of the following

✓ Bruising 1-2 times per month
✓ Epistaxis 1-2 times per month
✓ Frequent gum bleeding
✓ Family history of bleeding symptoms

COEIN

- Anovulation
- Age: peri-menarche and perimenopuse
- PCOS
- Stress
- Hypothyroidism
- Luteal phase defects

- Luteal Phase Defect (LPD)

✓ Luteal phase lasts 7-10 days (vs. 14 days) or inadequate peak luteal phase progesterone (P)

- Diagnosis

✓ Polymenorrhea (“periods every 2 weeks”)

✓ Mid-luteal phase P level between 4-8 ng/ml

✓ Endometrial biopsy >2 days out of phase

COEIN: Endometrial

- Idiopathic
- ✓ Unexplained menorrhagia
- Endometritis
- ✓ Post-partum
- ✓ Post-abortal endometritis
- ✓ Endometritis component of PID
- In teens, PID commonly presents with abnormal bleeding (menorrhagia, IMB), not pelvic pain
- Any teen with abnormal bleeding + pelvic pain requires bimanual exam to evaluate for PID

COEIN : Iatrogenic condition

- Anticoagulants

✓ Over-anticoagulation: menorrhagia

✓ Therapeutic levels will not cause bleeding problems

- Chronic steroids, opiates
- Progestin-containing contraceptives
- Intrauterine Contraception (IUC)

✓ "Normal" side effect menorrhagia

✓ PID, pregnancy (IUP or ectopic), perforation, expulsion

COEIN: Not Classified

- Chronic endometritis
- AVM
- Myometrial hypertrophy

Diagnostic management

- **History**

- Any known uterine disease, induced vaginal bleeding.

- Risk factors for hypothyroidism and any personal or family history of disorders of hemostasis must be sought with specific questions(Grade B)

History

- Age
- Age at menarche.
- Parity
- Menstrual History
- regularity, frequency, duration of bleeding , Volume of blood loss.
- Post coital bleeding ?
- Dysmenorrhoea –spasmodic / congestive
- Dyspareunia.
- O.H.---fertility / infertility/ gravidity / parity etc
- Associated Vaginal Discharge
- Recent Abortion / delivery / ectopic pregnancy .
- IUCD insertion , ocs, hormone therapy/ drugs.

Clinical Examination

- A complete clinical examination is recommended, including checking for signs of anemia, abdominal palpation, and a cervical examination, both digital and with a speculum , except for virgins or adolescents.

- When the history suggests nothing relevant, the pictogram is normal, the clinical examination is normal and no sign of anemia is present, no diagnostic investigation is recommended

laboratory Investigations

- CBC
- Blood coagulation profile
- TFT if there is any risk factors
- B HCG

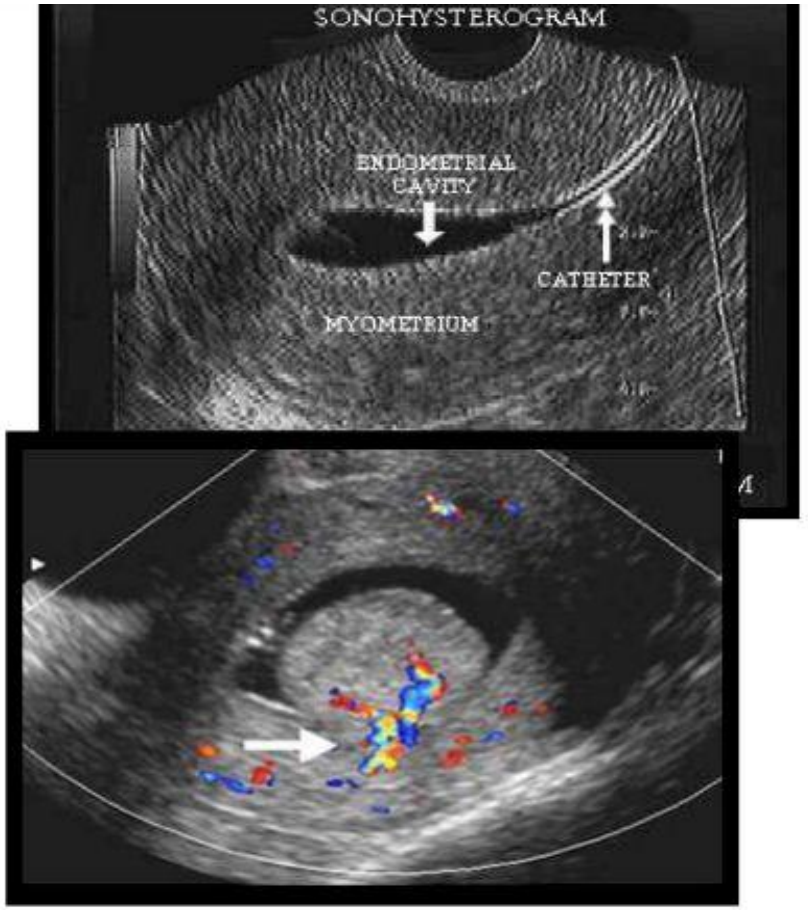
Imaging examinations

- Pelvic ultrasound: both abdominal and transvaginal, is recommended as a first-line procedure for the etiological diagnosis of AUB

- Doppler ultrasonography provides additional information useful for characterizing endometrial and myometrial abnormalities

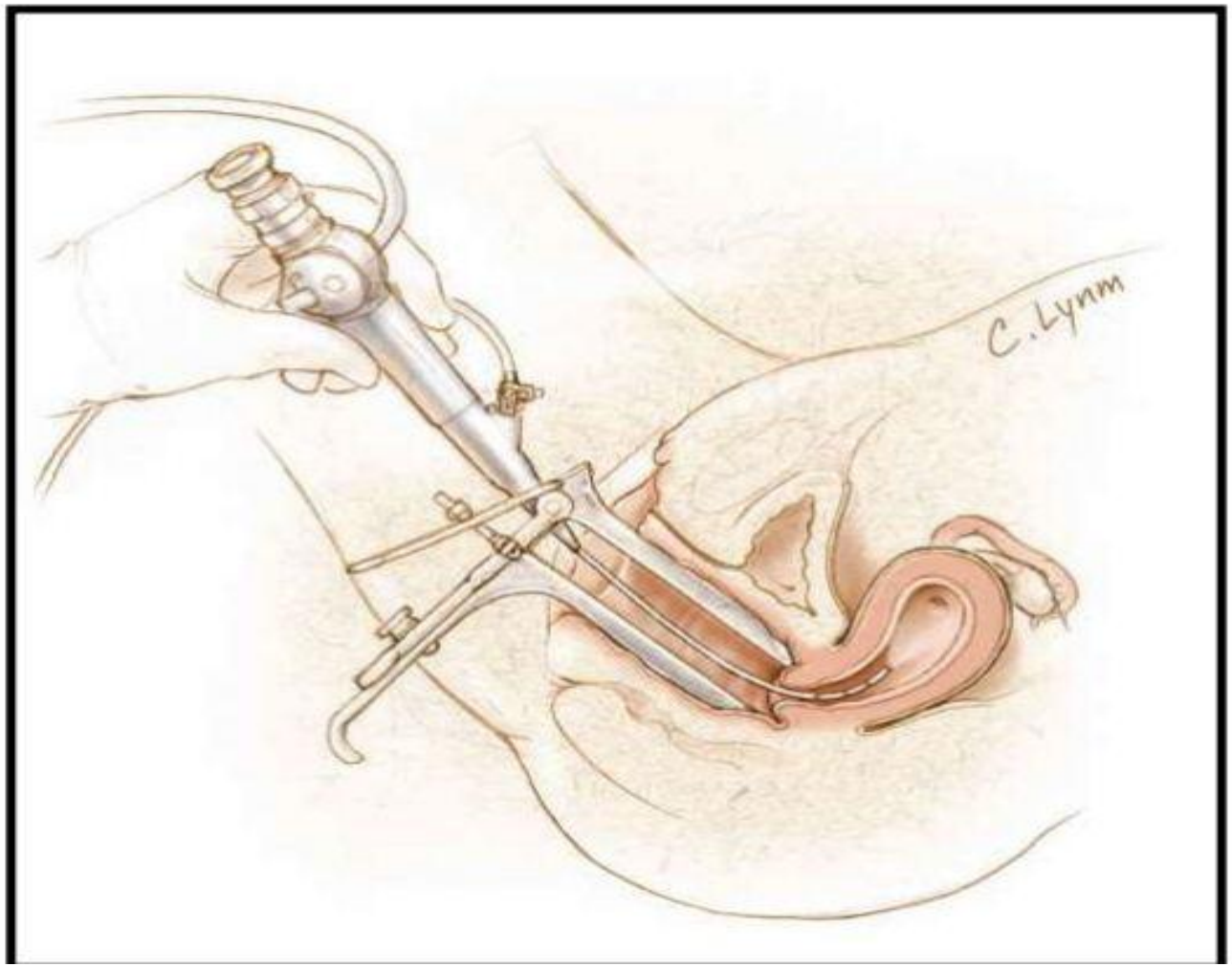
TVS & SIS

TVS



SIS

Hysteroscopy



Hysteroscopy or SIS

- Uterine exploration:

Hysteroscopy or SIS can be suggested as a second-line procedure when ultrasound suggests an intrauterine abnormality or if medical treatment fails after 3–6 months (Grade B)

Endometrial biopsy

- An endometrial biopsy must be performed in the case of any risk factor for endometrial cancer and for all patients older than 45 years
- A biopsy sample should be obtained with a polypropylene endometrial suction curette (Pipelle de Cormier)during the diagnostic hysteroscopy (Grade B)
- Diagnostic curettage under general anesthesia is not recommended as a first-line treatment
- Hysteroscopic directed biopsies

Treatment

- **A. General**

✓Treatment of iron deficiency anemia

- **B- Medical**
- **Non –hormonal**
- 1.Prostaglandin synthetase inhibitors (PSI) 2.Antifibrinolytics
- **Hormonal**:
- 1.Progestagen 2.Oestrogen 3.COCP 4.Danazol 5.GnRh agonist 6.Levo-nova (Mirena) II.
- **C. Surgical**
- 1 Endometrial ablation 2. UAE 3. Hysterectomy

Non hormonal drugs

Tranexamic acid

Competitive inhibitor of plasminogen activator
-antifibrinolytic agents

Menorrhagia
-Reduced breakdown of fibrin preformed clot in spiral endometrium arterioles → reduce MBL

Reduce MBL by 34-59%

However,
-not reduce dysmenorrhea
-not a contraceptive
-not regulate cycles

Cost effective when compared with other NSAIDS and no treatment
-not when compared with LNG-IUS

Dosage:
1g (2 tablets) 3-4x daily from onset of bleeding up to 4 days

Non hormonal drugs

NSAIDs

Reduce prostaglandin synthesis by inhibiting COX

Prostaglandin:
- Inflammatory response
- Pain pathways
- Uterine cramps
- Uterine bleeds

Treatment of dysmenorrhea

Reduces MBL 20-49% but tranexamic acid and danazol reduces MBL greater
-better AE profile than danazol

Less cost effective than LNG and tranexamic acid

However,
- Not contraceptions
- Not to be used in bleeding disorders

Non-Hormonal Drugs

- Tranexemic acid is more effective than NSAIDs
- But both can be used together
- And either can be continued long term if benefit is obtained
- But should be stopped if there is no response after 3 cycles
- Neither are contraceptive or cycle regulating
- NSAID is the drug of first choice when there is concomitant dysmenorrhoea
- All of the trials excluded women with fibroids so their role in menorrhagia with fibroids is uncertain

Systemic progestagens

- Norethisterone & medroxyprogesterone acetate
- Ovulatory DUB:

✓ not effective if given at low dose for short duration (5-10 days) in the luteal phase.

✓ Effective if NEA is given at higher dose for 3 w out of 4 w (5 mg tds from D5 to 26)

- Anovulatory DUB: useful Side effects: weight gain, nausea, bloating, edema, headache, acne, depression, exacerbation of epilepsy &

- Progestational Agents

✓ Cyclic medroxyprogesterone 2.5-10mg daily for 10-14 days

✓ Continuous medroxyprogesterone 2.5-5mg daily

✓ Progesterone in oil, 100mg every 1 week

✓ DepoProvera® 150mg IM every 3 months

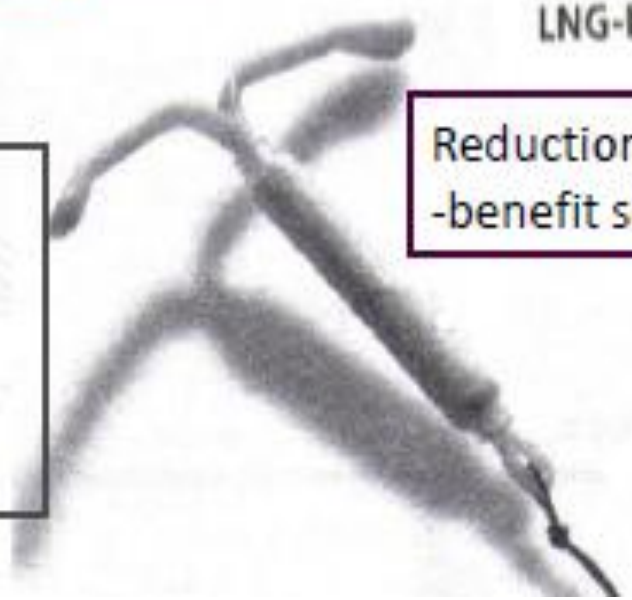
✓ Levonorgestrel IUD (5 years)

Levonorgestrol IUD

LNG-IUS

Vertical stem: release daily doses of 20 micrograms of LNG

Cost effective when compared with other hormonal and non hormonal treatments



Reduction of MBL between 71-96%
-benefit seen after 6 months

Effects:
-prevent endometrial proliferation
-thicken cervical mucus
-suppress ovulation

LNG-IUS(Mirena)

- **Effect**
- **Comparable** to endometrial resection for management of AUB.
- **Superior** to PSI & antifibrinolytics
- May be an **alternative** to hysterectomy in some patients

COCP

Contain estrogen and progestogen in combinations

Act on HPO axis to suppress ovulation and fertility
Endometrial suppresion
-cause withdrawal bleeding

Reduces MBL by 43 -50 %
- Greater than naproxen
- Lesser than danazol and tranexamic acid

Less benefit

OCP

- OCP Mechanism of action: endometrial suppression
- Side effects; headache, migraine, weight gain, breast tenderness, nausea, cholestatic jaundice, hypertension, thrombotic episodes,

GnRH-analogues

Synthetic peptide that act like a natural GnRH but with longer biological half life

No follicular development, estrogen production, no ovulation, no progeterone, no menses

Action

1. **Flare effect**
   -increase FSH and LH
2. **Profoung hypogonadal effect**
   - after 10 days downregulation

Treatment

1. Hormonal sensitive cancer
   -breast cancer, prostate cancer

2. Estrogen dependant lesion
   - leiomyoma, endometriosis

Reduces MBL but with high adverse effects

GnRH analog

- **Side effects**

✓hot flushes

✓Sweats

✓ headache

✓ irritability

✓ loss of libido

✓ vaginal dryness

✓ lethargy

✓reduced bone density

GnRh agonist

- Most studies have been directed at the reduction of uterine size with these agents that induce a “reversible menopause”
- Reductions in uterine size up to 75% over 6m can occur
- Up to 90% of patients achieve amenorrhea
- This can be very useful prior to hysterectomy
- Oestrogen-deficiency symptoms i.e. hot flushes, vaginal atrophy and bone loss are limiting
- But these can be overcome with add-back therepy using small doses of oral oestrogen, COC, progestin or tibilone • GnRH are currently very expensive drugs

Recommendations for pharmacological approach

- Considered in

✓no structural or histological abnormalities

✓ fibroid <3 cm that not distort uterus

- Choices depends on wish to conceive
- If either can, follow order

1. LNG-IUS
2. Tranexamic acid or COCP
3. Oral Progestogen

- If treatment is needed during investigations or before definite treatment - tranexamic acid or NSAIDs
- If coexist with dysmenorrhea choice is NSAIDs
- Stop NSAIDs and tranexamic acid if no improvement after 3 cycles
- GnRH-agonist is recommended prior to surgery
- other treatments of uterine fibroids (UAE, surgery) is contraindicated

Not to be used AUB treatment

- Danazol
- Oral progestogen during luteal phase

Surgical treatment

- Endometrial ablation Methods:

✓ Hysteroscopic:

1. Laser
2. Electrosurgical:

a. Roller ball

b. Resection

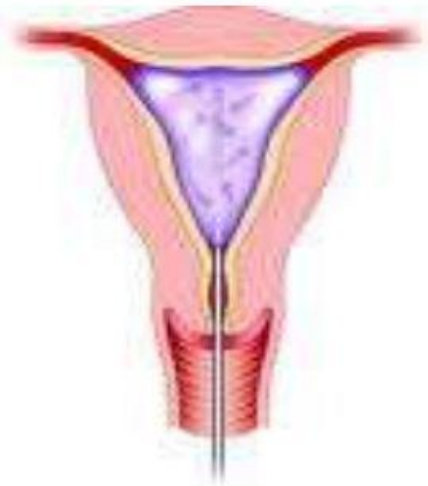
✓Non-hysteroscopic:

1. Thermachoice
2. Microwave

Indications:

- Failure of medical treatment
- Family is completed
- Uterine cavity<10 cm
- Submucos fibroid<5 cm
- Endometrium is normal or low risk hyperplasia.

Endometrial ablation



Thermal balloon ablation

Loop resection

Uterine artery embolization (UAE)

- **Indications**

✓ Heavy bleeding

✓Large fibroids

- **How it works?**

Small particles introduced into artery supply to the uterus and fibroid shrinks

- **Adverse outcomes**

✓ Persistent vaginal discharge

✓ Post-embolisation syndrome: pain, nausea, vomiting and fever

✓ Need additional surgery

✓Premature ovarian failure

✓ hematom

Hysterectomy

- **Indications**:

1. Failure of medical treatment
2. Family is completed

- **Routes**:

1. Abdominal
2. 2. Vaginal
3. Laparoscopic

Advantages and Disadvantages

- **Advantages**

✓Complete cure

✓ Avoidance of long term medical treatment

✓ Removal of any missed pathology

- **Disadvantages**

✓Major operation

✓Hospital admission

✓Mortality & morbidity