Diagnostic procedures for cervical and endometrial cancers

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Diagnostic procedures for cervical cancers

3rd most common cancer/world

Most common cause of death from cancer in women

80% of new cases in developing countries

(Parkin et al, 2000)
Diagnostic procedures for cervical precursor lesions

Causal relationship between persistent infection with high-risk HPV; prevalence HPV 99.7% (Walboomers et al 1999)

HPV 16 and 18 responsible for 70% of cervical cancers

Cervical cancer progresses slowly from preinvasive cervical intraepithelial neoplasia (CIN) to invasive cancer
Mean age 51 years  \textit{(Jemal et al 2009)}

Risk factors:
- Young age at first coitus (<20yrs)
- Multiple sexual partners
- Sexual partner with multiple sexual partners
- Young age at first pregnancy
- High parity
- Lower socioeconomic status
- Smoking
Diagnostic procedures for cervical precursor lesions

Screening of asymptomatic women

Annual physical examination
PAP smear: within 3 years of sexual intercourse or by age of 21
Annual screening until age 30 > 3 consecutive negative tests > every 2-3 yrs

False-negative rate 50% (higher for glandular lesions and invasive cancers) (Berman et al 1984)
Diagnostic procedures for cervical precursor lesions

PAP smear versus Thin Prep (automated liquid-based slide-preparation systems)

Advantage liquid-based systems:
- Blood, mucus and inflammatory cells eliminated
- Computerized image processors
- Cost-effectiveness
Diagnostic procedures for cervical precursor lesions

Colposcopy

Colposcopic hallmark of CIN:

- Sharply delineated acetowhite epithelium (acetic acid dehydrates cells > reflex from areas of increased nuclear density)
- Abnormal vascular patterns within acetowhite areas: punctuation, mosaicism
- Microinvasive carcinoma: extremely irregular punctuate and mosaic patterns, small atypical vessels
- Frank cancer: comma-shaped vessels, corkscrew-shaped and dilated, blind-ended vessels
Diagnostic procedures for cervical precursor lesions

Punch biopsy
<table>
<thead>
<tr>
<th>Pap München</th>
<th>WHO</th>
<th>CIN</th>
<th>Bethesda</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Normal</td>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td>IIW</td>
<td>HPV Infect, unclear lesion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Unclear</td>
<td></td>
<td>ASC-US/AGUS</td>
</tr>
<tr>
<td>IIID</td>
<td>Mild Dysplasia</td>
<td>CIN 1</td>
<td>Low Grade/LSIL</td>
</tr>
<tr>
<td>IIID</td>
<td>Intermediate Dysplasia</td>
<td>CIN 2</td>
<td>High Grade/HSIL</td>
</tr>
<tr>
<td>IVa</td>
<td>Severe Dysplasia</td>
<td>CIN 3</td>
<td>High Grade/HSIL</td>
</tr>
<tr>
<td>IVa</td>
<td>Carcinoma in situ</td>
<td>CIN 3</td>
<td>High Grade/HSIL</td>
</tr>
<tr>
<td>IVb</td>
<td>Microinvasive Carcinoma</td>
<td></td>
<td>Carcinoma</td>
</tr>
<tr>
<td>V</td>
<td>Invasive Carcinoma</td>
<td>Cancer</td>
<td>Carcinoma, invasive</td>
</tr>
</tbody>
</table>
CIN III 6 and 9 o’clock

Aceto acid

Iodine
CIN III 2 and 5 o’clock

Aceto acid

Iodine
AGC-N (cytology), Adenocarcinoma in situ (biopsy)

Aceto acid

Iodine
Diagnostic cone biopsy

- Persistent CIN I for years (remission 55%, progression 15%)
- Persistent CIN II > 3 mth (remission 40%, progression 20-30%)
- CIN III, CA in situ (remission 10%, progression 50-70%)

(CME Springer 2012)
Laser conisation

Advantage:
- small conus

Disadvantage:
- Expertise/Training
- high costs for equipment
- hard to investigate margins
LLETZ/LEEP

Advantage:
- local anaesthesia - outpatients
- low blood loss
- short procedure

Disadvantage:
- hard to investigate margins
- necessary to take cone in pieces if loop to small
Cold knife cone biopsy

Advantage:
- excellent to see margins

Disadvantage:
- blood loss
- Intubation necessary

Indication:
- Microinvasive carcinoma
- severe glandular changes
- Adeno-Ca in situ
Diagnostic procedures for **cervical cancers**

**Symptoms**

- Most common: abnormal vaginal bleeding (56%)
- Abnormal PAP smear (28%)
- Sexually active women: postcoital bleeding
- Large tumors become infected: serous, purulent, malodourous or bloody discharge (4%)
- Pelvic pain (9%), leg swelling, urinary frequency
- In developing countries not uncommon: fistula formation

*(Pretorius et al 1991)*
SCC Cervix
Diagnostic procedures for cervical cancers

FIGO clinical staging

- Examination under anaesthesia (Rectovaginal examination: diameter, spread to parametria, extension into uterosacral ligaments)

  +/-
  - Biopsies
  - Cystoscopy
  - Sigmoidoscopy
  - Chest/skeletal X-Ray
  - IVP
  - Liver function test
Diagnostic procedures for cervical cancers

Imaging

- **MRI** single best modality for evaluation; helpful for management planning:
  - extent primary lesion (for tumors >2cm)
  - extension into parametrium (Sens 70-100% vs. 50% in CT scans)
  - bladder or rectum involvement (Sens 83%, accuracy 99%) *(Schmid 2013, Kim 2011)*

- **PET/CT** > *lymph node metastases* (single most important prognostic factor: 20% positive PA LND in Stage II, 30% in Stage III)
  - Pelvic/para-aortic LND: Sens 75-85%, PPV 75% *(Leseur 2011, Antonsen 2013)*
Diagnostic procedures for endometrial cancers
Diagnostic procedures for endometrial cancers

Most common malignancy of female genital tract in Western world; Mean age 50 – 70 years

Most cases diagnosed at early stage when surgery alone may be adequate for cure

5-yr survival rates

- localized disease 96%
- regional disease 67%
- metastatic disease 26%
Diagnostic procedures for endometrial cancers

Symptoms

- Postmenopausal bleeding
- Postmenopausal patient with pyometra
- Asymptomatic woman with abnormal endometrial cells on Pap smear > 25% have EC (Zucker et al 1984)
- Perimenopausal patient with abnormal bleeding, esp. in a Hx of anovulation (obesity, polycystic ovaries)
- Perimenopausal woman with intermenstrual bleeding or increasingly heavy periods
Diagnostic procedures for endometrial cancers

Etiology of abnormal bleeding (in 90% of women with endometrial cancer)

- Exogenous hormones 30-10%
- Atrophic endometritis/vaginitis 30%
- Endometrial CA 15%
- Endometrial/cervical polyps 10-30%
- Endometrial hyperplasia 5%
- Misc (Cervical CA, uterine sarcomas, urethral caruncle, trauma) 10%

(Hacker et al 2004)
# Diagnostic procedures for endometrial cancers

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Type I cancers (80%)</th>
<th>Type II cancers (20%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristics</strong></td>
<td>Estrogen-related, low-grade endometrioid, associated with atypical endometrial hyperplasia, ER/PR positive</td>
<td>Unrelated to estrogen or endometrial hyperplasia, high grade tumors, poor prognostic cell types such as serous, clear cell and mucinous tumors, ER/PR negative</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td>Endogenous estrogen (obesity, anovulatory cycles, estrogen secreting tumors); exogeneous estrogen (unopposed HRT, Tamoxifen)</td>
<td>multiparous</td>
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<tr>
<td></td>
<td>Diabetes mellitus, Hypertension</td>
<td></td>
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<td></td>
<td>Age postmenopausal &gt;60</td>
<td>Older than Type I cancer pts</td>
</tr>
<tr>
<td></td>
<td>Family History (HNPCC, BRCA)</td>
<td>Family history of breast cancer</td>
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<td></td>
<td>Diet (high amount of fat)</td>
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<tr>
<td><strong>Mutations</strong></td>
<td>PTEN (40-50%), MSI (20-30%), KRAS2 (10-30%)</td>
<td>P53 (70-90%), Ki-67</td>
</tr>
</tbody>
</table>
Diagnostic procedures for endometrial cancers

Pre-operative evaluation

**Pipelle de Cornier** best device

- Endometrial CA Diagnosis: Meta-analysis: Sens 99.6% postmenopausal, 91% premenopausal, specificity 98% *(Dijkhuizen et al., 2000)*
- False negative rate 10%
- **Hysteroscopy with dilation and curettage (D&C)** remains **gold standard**
- Tumor grade often undergraded at D&C
  - Sens. **G1** Pipelle and D&C 93.8% and 97%;
  - **G3** Pipelle and D&C 99.2% and 100%; *Huang et al. 2011*
Diagnostic procedures for endometrial cancers

Transvaginal ultrasonography

EC has endometrial thickness 18.2 +/- 6.2mm (Granberg et al 1991)
100% of cancers and 95% of hyperplasia had ET >5mm (Saccardi 2013; Chandavarkar 2013)

>>> persistent postmenopausal bleeding in the setting of normal sonographic findings requires endometrial sampling!
Diagnostic procedures for endometrial cancers

Sonohysterography
Premenopausal women
Determination of polypoid lesions
for resection via hysteroscopy

Hysteroscopy and fractional curettings
First fractional curettage with ECC to rule out endocervical cancer
False positive endocervical curettage for Stage II: 40-50%
If diagnosis expanded and ECC negative > wedge or cone biopsy
Diagnostic procedures for endometrial cancers

Screening

• General population: no studies confirming efficacy

• Women at risk of HNPCC:
  • 40-60% risk for endometrial cancer
  • 12% lifetime risk for ovarian cancer
  • American Cancer Society: annual screening by endometrial biopsy from age 35 (at present no data regarding efficacy of this approach)
  • Prevention ? Prophylactic TLH, BSO

• Women taking Tamoxifen: no atypia <5mm; US 5mm cut-off shows 100% sensitivity > no difference in surveillance (Saccardi 2013)
Diagnostic procedures for endometrial cancers

Imaging unnecessary in G1 cancers

CT-scan:
May be helpful to determine extent of metastatic disease
- Rarely alters treatment and is expensive
- Unnecessary unless suspicion of extrapelvic disease, poor predictor of nodal disease, depth of invasion and cervical involvement
Diagnostic procedures for endometrial cancers

**Contrast-enhanced MRI:**
Best radiographic modality for assessing myometrial invasion and cervical involvement *(meta-analysis Kinkel et al 1999)*; better than CT or US
- More accurate for LND metastases
- Better for myoinvasion (detection in 90%, PPV 92% versus CT 64% and US 40%)

**PET/CT:** myometrial invasion 93% Sens (MRI 87%), cervical invasion 43% Sens (MRI 33%), LN mets 74% Sens, MRI 59% *(Antonsen 2013)*
Diagnostic procedures for endometrial cancers

**Tumormarker CA125**
Clinically useful test for predicting extrauterine spread
Correlates with
- Advanced stage
- Positive lymph node status
- Follow-up after initial treatment

- CA125>65 was most significant predictor of extra-uterine disease (6.5x higher risk (Sens 62%, Spec 91%, PPV 69%) Sood et al 1997
Meier et al., Gynaecol Oncol 2011
Conclusions

• Up to CINII regression is possible
• Cervical punch and cone biopsy essential
• Cervical cancer needs clinical staging

• Pipelle de Cornier effective and cheap method of sampling
• No need to screen with CA125
Thank you for your attention