Abnormal Cervical Cytology Management

Normal
ASCUS
Low-Grade
High-Grade
Squamous

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Cervical cancer;

- The second most common cancer among women in the world
- In 2017, 11,080 new invasive cervical cancers were diagnosed in the United States; 2980 deaths
Abnormal Cervical Cytology Management

Transient Infection
- HPV
- Initial infection
- Normal cervix
- HPV-infected cervix
- Clearance
- Mild cytologic abnormalities

Persistent HPV Infection
- Progression
- Regression
- Precancerous lesion
- Invasion
- Cancer

3 - 5 Year

Abnormal Cervical Cytology Management

Age 10 15 20 30 40 50

Menarche (13)
Sexual age (18)
HPV Contact (21)
CIN 1 (22)
CIN 3 (23)
Persistent CIN 3 (35)
Microinvasive Cx Ca (42)
Cx Ca (49)

27.04.2018

TAJEV 2018
Abnormal Cervical Cytology Management

<table>
<thead>
<tr>
<th>Tests</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>Cytology</td>
<td>%53</td>
<td>%97</td>
</tr>
<tr>
<td>HPV test</td>
<td>%96</td>
<td>%92</td>
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HPV vs. Cytology sensitivity

Cumulative CIN3+ Incidence by Tests
## Abnormal Cervical Cytology Management

<table>
<thead>
<tr>
<th>Pap</th>
<th>WHO</th>
<th>CIN</th>
<th>Bethesda</th>
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<tbody>
<tr>
<td>Class I</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
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<tr>
<td>Class II</td>
<td>Atipik enf.</td>
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<td>Benign veya ASC</td>
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<td>ASC-US</td>
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<tr>
<td>Class III</td>
<td>Displazi</td>
<td>CIN 1</td>
<td>SIL</td>
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<tr>
<td></td>
<td>Weak</td>
<td></td>
<td>LGSIL</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>CIN 2</td>
<td>HGSIL</td>
</tr>
<tr>
<td>Class IV</td>
<td>Hard</td>
<td>CIN 3</td>
<td></td>
</tr>
<tr>
<td>Class V</td>
<td>CIS</td>
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What is Abnormal PAP Smear?

- Abnormal due to inadequacy
- Abnormal due to inflammation
- Abnormal due to infection
- Abnormal due to dysplastic changes
Abnormal Cervical Cytology Management

- Squamous Cell
- **ASC (Atypical Squamous Cells)**
  - ASC-US (ASC-Undetermined Significance)
  - ASC-H (Can not exclude High grade lesion)
- **LGSIL (Low Grade Squamous Intraepithelial Lesion)**
- **HGSIL (High Grade Squamous Intraepithelial Lesion)**
- Glandular Cell
- **AGC (Atypical Glandular Cells)**
  - AGC-NOS (AGC-Not Otherwise Specified)
  - AGC-Favor Neoplasia
  - AIS (Endocervical Adenocarcinoma In Situ)
Unsatisfactory Cytology

- < % 1
- Insufficient number of squamous cells
- Co-test HPV (-)
- Not safe
- Liquid based cytology
- Treat atrophy and inflammation
**Unsatisfactory Cytology**

- **HPV unknown (any age)**
  - Abnormal: Manage per ASCCP Guideline
  - Negative: Routine screening (HPV-/unknown) or Cotesting @ 1 year (HPV+)

- **HPV negative (age ≥30)**
  - Repeat Cytology after 2-4 months
  - Negative: Routine screening (HPV-/unknown) or Cotesting @ 1 year (HPV+)

- **HPV positive (age ≥30)**
  - Repeat Cytology after 2-4 months
  - Unsatisfactory: Colposcopy
Cytology (-) but EC / TZ Absent/Insufficient

- Inadequate sampling of SC component
- % 10-20
- Higher in elderly population
- Risk of CIN 3+ lesion in elderly population is low
- After CIN 2+ treatment, there is no risk increase even if EC / TZ (-)

Zhao C, Gynecol Oncol 2007;107:231-5.
Cytology NILM* but EC/TZ Absent/Insufficient

- Ages 21-29+
  - HPV negative
    - HPV testing (Preferred)
  - HPV unknown
    - Repeat cytology in 3 years (Acceptable)
- Age ≥30 years
  - HPV positive
    - Cytology + HPV test in 1 year
    - Genotyping
  - HPV negative or HPV unknown
    - Manage per ASCCP Guideline
- Routine screening

*Negative for intraepithelial lesion or malignancy
*HPV testing is unacceptable for screening women ages 21-29 years

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Cytology (-) HPV (+)

- Co-test between 30-64 years
- CIN 3+ risk is high in those with HPV (+)
- There is a risk of recurrent HPV (+)
- Type 16 (+) associated with CIN 3+
- Type 18 is associated with adenocarcinoma (more difficult to detect with cytology)
Management of Women ≥ Age 30, who are Cytology Negative, but HPV Positive

- Repeat Cotesting @ 1 year
  Acceptable

  - Cytology Negative and HPV Negative
    - Repeat cotesting @ 3 years

  - ≥ASC or HPV positive

- HPV DNA Typing Acceptable

  - HPV 16 or 18 Positive
    - HPV 16 and 18 Negative
      - Repeat Cotesting @ 1 year

  - Manage per ASCCP Guideline

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• 1/3 - 2/3 of cases are unrelated to HPV
• 5 year CIN 3+ risk 3%
• > 65 yaş HPV(-) ASC-US continue scanning with sitio or co-test
• ASC-US ve HPV 16,18(+) CIN 3+ riski 2 kat artar
• Prefer refleks test
• HPV(-) ASC-US after 3 years co-test
• HPV(+) ASC-US Colposcopy
• LEEP = over-treatment
• Colposcopy at 6th week after birth in pregnancies, dont make ECC
LSIL

- HPV (+) % 77
- If make Co-test (> 30 y) HPV(-) LSIL, CIN 3+
- 21-24 year LSIL CIN3+
- 25-29 year olds are approached to LSIL with no HPV test (colpos.)
- Colposcopy is done in pregnancy immediately after birth at 6th week
- Postmenopausal LSIL dont make HPV test; Co-testing and colposcopy at 6th and 12th months
Management of Women with Low-grade Squamous Intraepithelial Lesions (LSIL)*†

- **LSIL with negative HPV test among women ≥ 30 with cotesting**
  - Preferred
  - Repeat Cotesting @ 1 year

- **LSIL with no HPV test**
  - Acceptable
  - Cytology Negative and HPV Negative
    - Repeat Cotesting @ 3 years
  - ≥ ASC or HPV positive
    - Colposcopy
      - Non-pregnant and no lesion identified
      - Inadequate colposcopic examination
      - Adequate colposcopy and lesion identified
        - Endocervical sampling “preferred”
        - Endocervical sampling “preferred”
        - Endocervical sampling “acceptable”

- **LSIL with positive HPV test among women ≥ 30 with cotesting**
  - No CIN2,3
    - Manage per ASCCP Guideline
  - CIN2,3
    - Manage per ASCCP Guideline

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* Management options may vary if the woman is pregnant or ages 21-24 years
† Manage women ages 25-29 as having LSIL with no HPV test
Management of Women Ages 21-24 years with Low-grade Squamous Intraepithelial Lesion (LSIL)

Women ages 21-24 years with LSIL

Repeat Cytology @ 12 months Preferred

Negative, ASC-US or LSIL

Negative x 2

ASC-H, AGC, HSIL

Repeat Cytology @ 12 months

≥ ASC

Routine Screening

Colposcopy

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Management of Pregnant Women with Low-grade Squamous Intraepithelial Lesion (LSIL)

Pregnant Women with LSIL

- Colposcopy
  Preferred
  - No CIN2,3^
    - Postpartum follow-up
  - CIN2,3
    - Manage per ASCCP Guideline

- Defer Colposcopy
  (Until at least 6 weeks postpartum)
  Acceptable
  ^ In women with no cytological, histological, or colposcopically suspected CIN2,3 or cancer
ASC - H

- Risk comparison; CIN 3+ > ASC-US, LSIL, < HSIL
- 21-24 year CIN 3+ risk < 25-29 year
- Don't make Refleks test
- HPV(-) ASC-H; 5-year cancer risk 2%
- 21-24 year colposcopy, don't make LEEP firstly
Management of Women with Atypical Squamous Cells: Cannot Exclude High-grade SIL (ASC-H)*

Colposcopy
Regardless of HPV status

No CIN2,3

- Manage per ASCCP Guideline

CIN2,3

- Manage per ASCCP Guideline

* Management options may vary if the woman is ages 21-24.
Management of Women Ages 21-24 yrs with Atypical Squamous Cells, Cannot Rule Out High Grade SIL (ASC-H) and High-grade Squamous Intraepithelial Lesion (HSIL)

- **Colposcopy**
  - (Immediate loop electrosurgical excision is unacceptable)
- **No CIN2,3**
- **CIN2,3**

- **Observation with colposcopy & cytology**
  - @ 6 month intervals for up to 2 years
  - **ECC(-)**
  - High-grade colposcopic lesion or HSIL
    - Persists for 1 year
  - Biopsy
  - Manage per ASCCP Guideline for young women with CIN2,3

- **Two Consecutive Cytology Negative Results**
  - and No High-grade Colposcopic Abnormality
  - Routine Screening

- **Other results**
  - Manage per ASCCP Guideline
  - Diagnostic Excisional Procedure
    - (if no CIN2,3, continue observation)

*If colposcopy is adequate and endocervical sampling is negative. Otherwise a diagnostic excisional procedure is indicated.

*Not if patient is pregnant
• In colposcopy, 60% of CIN 2+ 2% cervical cancer
• Immediate LEEP - an option to 'see and treat'
• Don't make Refleks test
• If colposcopy is insufficient diagnostic excision
• 21-24 year-old cancer risk is low, don't make LEEP
• > 30 years 5-year cancer risk 8%
• HPV (-) HSIL 5-year CIN 3+ risk 29%, cancer risk 7%
• HPV (+) HSIL 5-year CIN 3+ risk 50%, cancer risk 7%
Management of Women with High-grade Squamous Intraepithelial Lesions (HSIL)*

Immediate Loop Electrosurgical Excision*  Or  Colposcopy (with endocervical assessment)

No CIN2,3  CIN2,3

Manage per ASCCP Guideline

* Management options may vary if the woman is pregnant, postmenopausal, or ages 21-24
* Not if patient is pregnant or ages 21-24

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• Associated with polyps, metaplasia and adenocarcinomas
• AGC-favor neoplazi, AIS; neoplazi high risk
• <35 years AGC, CIN 2+ high risk, cancer risk
• > 30 years AGC, CIN 3+ risk 9%, cancer risk 3%
• 50% of AIS cases have CIN available
• Reflex test HPV (-) is the risk of endometrial cancer
• Benign endometrial cell, stromal cell or histiocyte risk of endometrium cancer in 5% of postmenopausal women
Initial Workup of Women with Atypical Glandular Cells (AGC)

- All subcategories (except atypical endometrial cells)
  - Colposcopy (with endocervical sampling)
  - Endometrial sampling (if ≥ 35 yrs or at risk for endometrial neoplasia*)

- Atypical Endometrial Cells
  - Endometrial and Endocervical Sampling
    - No Endometrial Pathology
      - Colposcopy

*Includes unexplained vaginal bleeding or conditions suggesting chronic anovulation.
Subsequent Management of Women with Atypical Glandular Cells (AGC)

**Initial Cytology is AGC - NOS**

- **No CIN2+, AIS or Cancer**
  - Cotest at 12 & 24 months
    - Both negative: Cotest 3 years later
    - Any abnormality: Colposcopy

- **CIN2+ but no Glandular Neoplasia**
  - Manage per ASCCP Guideline

**Initial Cytology is AGC (favor neoplasia) or AIS**

- **No Invasive Disease**
  - Diagnostic Excisional Procedure
    - *Should provide an intact specimen with interpretable margins. Concomitant endocervical sampling is preferred*

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• Even if HPV (-) is inadequate smear should be repeated
• Sito (-) TZ (-) is not required immediately smear repetition
• Over 30 years old Sito (-) HPV (+); Co-test after 1 year
• ASC-US HPV (+) is colposcopy
• ASC-US HPV (-) co-test after 3 years
• ASC-US should continue to scan after 65 years old even if HPV (-)
• 21-24 years younger women are treated more conservatively
• Avoid invasive procedures in pregnancy.
Take home Messages

- Patient anxiety should be reduced
- Physician's patient; abnormal smear = cancerous perception
- Good counseling should be provided
- There should be no indication of abnormal smear hysterectomy
- If you need colposcopic examination, you should go to experienced centers
Thanks...