Screening Women for Anal Cancer

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Disclosures

- No financial relationships or conflict of interest to disclose
Objectives:

• Identify WHO is at increased risk for anal cancer
• Review anal HPV in women and in anal cancer
• Learn to assess for anal cancer with history and physical exam— the perianus and digital anal rectal exam (DARE)
• Consider other anal cancer screening modalities: anal cytology/HPV testing/High resolution anoscopy
Anal cancer risk in women
CERVICAL AND ANAL CANCER INCIDENCE (USA, SEER data)

http://seer.cancer.gov/
Non-anal HPV associated cancers/conditions and anal cancer risk

SIR for anal cancer

- Vulvar cancer: 45.5
- CIN3: 5.9-6.7
- Cervical cancer: 6.3
- Condyloma: 7.8-9

Stier, Am J Ob Gyn, 2015; Moscicki, JLGTD, 2015
Immunosuppression in women and anal cancer risk

HIV infection

(SIR 18-47)

Solid organ transplant

(SIR 5.4)

Stier, Am J Ob Gyn, 2015; Moscicki, JLGTD, 2015
Age and anal cancer risk?
SEER Incidence Rates by Age at Cancer Diagnosis, 2010-2014

Incidence per 100,000

Age at diagnosis

CERVIX

ANUS

http://seer.cancer.gov/
SEER Incidence Rates by Age at Cancer Diagnosis, 2010-2014

Incidence per 100,000

Age at diagnosis

CERVIX

ANUS

http://seer.cancer.gov/
Risk of anal cancer in women with a history of CIN3, by age
(Swedish Cancer Registry)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>CIN3 with anal cancer</th>
<th>No h/o CIN3 with anal cancer</th>
<th>Anal cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>n</td>
<td>IRR (95% CI)</td>
</tr>
<tr>
<td>18–29 years</td>
<td>1</td>
<td>6</td>
<td>31.1 (3.7–258.4)</td>
</tr>
<tr>
<td>30–39 years</td>
<td>7</td>
<td>32</td>
<td>7.6 (3.3–17.2)</td>
</tr>
<tr>
<td>40–49 years</td>
<td>29</td>
<td>118</td>
<td>5.8 (3.9–8.8)</td>
</tr>
<tr>
<td>50–59 years</td>
<td>44</td>
<td>229</td>
<td>4.7 (3.4–6.5)</td>
</tr>
<tr>
<td>≥ 60 years</td>
<td>50</td>
<td>472</td>
<td>4.0 (3.0–5.3)</td>
</tr>
</tbody>
</table>

IRR = incident rate ratios

Edgren G, Lancet Oncol 2007
Risk of anal cancer in women with a history of CIN3, by years since diagnosis (Swedish Cancer Registry)

<table>
<thead>
<tr>
<th>Years since CIN3 diagnosis</th>
<th>Anal cancer</th>
<th>Events (n)</th>
<th>IRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–4 years</td>
<td></td>
<td>4</td>
<td>1.7 (0.4–4.4)</td>
</tr>
<tr>
<td>5–9 years</td>
<td></td>
<td>12</td>
<td>3.9 (2.1–6.6)</td>
</tr>
<tr>
<td>≥10 years</td>
<td></td>
<td>115</td>
<td>5.0 (4.1–6.0)</td>
</tr>
<tr>
<td>No CIN 3 history</td>
<td></td>
<td>857</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Edgren G, Lancet Oncol 2007
Anal cancer incidence in HIV+ persons by age, sex and sexual orientation

Incidence per 100,000 p-y

Age range

Colon-Lopez, JCO, 2017
At what age are women at increased risk for anal cancer?

Age 40-45+  At risk patient populations?

Age 50 or 55+  All women?
WHO IS AT INCREASED RISK FOR ANAL CANCER?

- women age 45+ with...

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>INCIDENCE / 100,000 P-Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+ WOMEN</td>
<td>18-47</td>
</tr>
<tr>
<td>Vulvar cancer</td>
<td>46</td>
</tr>
<tr>
<td>Solid organ transplant</td>
<td>5</td>
</tr>
<tr>
<td>CERVICAL CANCER</td>
<td>6</td>
</tr>
<tr>
<td>CIN3</td>
<td>6-7</td>
</tr>
</tbody>
</table>

Darragh, Cancer Cytopath, 2011; Stier, AJOG, 2015; Moscicki, JLGTD, 2015
What do we know about women and anal HPV and anal cancer?
Hawaii Women Cohort study: HPV DNA detection by age and site (anus/cervix)

Hernandez, CEBP, 2005
Anal HPV prevalence in women by anal diagnosis and HIV status

Lin, Lancet Infectious Disease, 2017
Prevalence of HPV type in men by anal diagnosis and HIV status

Lin, Lancet Infectious Disease, 2017
Anal cancer and cervical cancer are very similar

• Strongly associated with HPV
• Association with HSIL
• Similar histology
• Arise in the transformation zone
LIKELY natural history
ANAL HPV infection $\rightarrow$ CANCER

ANAL HPV

HSIL AIN 2-3

CANCER

LSIL AIN1/condyloma
Age and prevalence HPV to CANCER in the cervix

Schiffman M et al. JNCI J Natl Cancer Inst 2011;jnci.djq562
LIKELY natural history
ANAL HPV infection → CANCER

Anal HPV ↔ HSIL/AIN2-3 → Anal cancer

Population prevalence by age
HIGH WITH MINIMAL CHANGE

??????????
INCREASES THROUGH LIFETIME

ASCP
Improving Lives Through the Prevention & Treatment of Anogenital & HPV-Related Diseases

ASCCP 2018 Annual Meeting
Why screen for anal cancer in women?
Anal cancer 5 year survival by stage at diagnosis

Earlier stage has better prognosis!

https://www.cancer.gov/
Standard of care for treatment for anal cancer is chemoradiation EVEN for localized disease*

* Except possibly for superficial invasive squamous cancer of the anus (SISCA)
The anus
How to “screen…”

**History—**

- Risk factors
- Symptoms*
  - anal pain/itching
  - anal bleeding
  - anal mass

*If symptomatic, no longer screening
Perianal itching ➔ “Psoriasis”
Physical exam—

• Examine the peri-anus
• Digital anal rectal exam (DARE)
The “hemorrhoid”
Perianal condyloma

Perineum

Post perianal

AIN 2

P-AIN 2
Diagnosis of Anal Carcinoma – Doctor’s Finger Still the Best?

Tanden, Oncology, 1991
Digital anal/rectal exam

DARE

BLADDER

URETHRA

ANUS

RECTUM

VAGINA

UTERUS

http://teachmeanatomy.info/
Cost-effective for HIV+ MSM 50+ at “regular intervals”, e.g. annually or q2-3 years

Ong, JIAS, 2016
SCREENING TESTS APPLY TO ASYMPTOMATIC PATIENTS

SYMPTOMS OF ANAL CANCER ➞ 
ANAL BLEEDING, PAIN OR MASS

邈 IF PRESENT, THEN CONSIDER REFER FOR HRA OR COLORECTAL SURGEON.

Note that a NORMAL COLONOSCOPY DOES NOT RULE OUT ANAL CANCER
HOW DOES ANAL CANCER SCREENING WORK?
SECONDARY PREVENTION

Abnormal screening test (e.g. cytology)

COLPOSCOPIC EVALUATION TO IDENTIFY IN2+ (HSIL)

TREATMENT OF IN2+ (HSIL) TO PREVENT PROGRESSION TO CANCER
What are possible “screening” tests?

Anal cytology?
Anal HPV?
Anal cytology?  Anal HPV?

WARNING--
Do not even consider these screening tests unless referral for high resolution anoscopy (HRA) is available!
Anal cytology
ANAL CYTOLOGY,
aka THE ANAL “PAP’ —

2cm
(1-3.2cm)*
Any abnormal anal cytology result → Refer for High Resolution Anoscopy (HRA)

<table>
<thead>
<tr>
<th>Abnormal results</th>
<th>Negative for intraepithelial lesions or malignancy (NILM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ASCUS</td>
</tr>
<tr>
<td></td>
<td>LSIL</td>
</tr>
<tr>
<td></td>
<td>ASC/H, HSIL</td>
</tr>
<tr>
<td>Cancer</td>
<td>AIN 2, AIN 3</td>
</tr>
</tbody>
</table>

Any abnormal anal cytology result → Refer for High Resolution Anoscopy (HRA)
What about screening with anal HPV?
Anal HPV is very common in women of ALL ages

Incident HPV infection and age—Healthy female Hawaii cohort

Goodman, Cancer Res, 2008
Goodman, JID, 2008
But testing for HPV 16 might be effective
Secondary screening assumes: Treating anal HSIL will prevent progression to anal cancer
However, we do not know if treatment of AIN2,3 will prevent anal cancer
To answer this question:
Anal Cancer HSIL Outcomes Research Study
ANCHOR Study –

PRIMARY OBJECTIVE
To determine whether treating anal HSIL is effective in reducing the incidence of anal cancer in HIV-infected men and women
In sum:

Anal cancer risk is highest in women age 40-45+ with:

• h/o vulvar or cervical cancer or pre-cancer
• Immunosuppression
In sum:

Anal cancer risk is highest in women age 40-45+ with
- h/o vulvar or cervical cancer or precancer
- Immunosuppression

Screen these women with
- Queries re: anal bleeding, pain, mass
- Careful perianal and digital anal rectal exam (DARE)
- IF HRA is available, consider anal cytology or direct referral for HRA
Thank you!

QUESTIONS?
elstier@bu.edu