Use of pelvic ultrasound screening in postmenopausal women

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U.Z. Leuven
Screening?

**MASS SCREENING**

This is a term used to indicate the large-scale screening of **whole population** groups.

**SELECTIVE SCREENING**

We use this term for the screening of **selected high-risk groups** in the population.

Mass Screening

- High incidence
- High mortality / morbidity
- Treatable Precursor
- Screening Test available
  - Accurate
  - Patient friendly
  - Low cost
Pelvic ultrasound screening

... for what?

- Endometrial cancer?
- Ovarian cancer?
- Uterine sarcoma?
- ...
Mass Screening: for endometrial cancer?

- Incidence  
  → 25 / 100 000

- High mortality / morbidity?  
  → 80% 5 year survival\(^{(1)}\)
  - Type 1\(^{(2)}\): estrogen-related (endometroid)
  - Type 2\(^{(2)}\): non-estrogen-related (serous- & clear cell CA)

- Treatable Precursor
  - For type 1 endometrial CA  
    → atypical hyperplasia (EIN)\(^{(3)(4)}\)
  - For type 2 endometrial CA  
    → ?? (serous EIC)\(^{(5)}\)

- Screening Test?
  - Ultrasound?

<table>
<thead>
<tr>
<th>Stage</th>
<th>5-year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>85%</td>
</tr>
<tr>
<td>II</td>
<td>75%</td>
</tr>
<tr>
<td>III</td>
<td>45%</td>
</tr>
<tr>
<td>IV</td>
<td>25%</td>
</tr>
</tbody>
</table>

Mass Screening: for **ovarian** cancer?

- Incidence: $\Rightarrow 21 / 100\,000^{(1)}$
- High mortality / morbidity?: $\Rightarrow 50\%\ 5$-year survival$^{(2)}$
- Treatable precursor?: **NO**
- Screening Test?
  - Ultrasound?
  - CA 125?

<table>
<thead>
<tr>
<th>Stage</th>
<th>5-year survival$^{(3)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>89%</td>
</tr>
<tr>
<td>II</td>
<td>66%</td>
</tr>
<tr>
<td>III</td>
<td>34%</td>
</tr>
<tr>
<td>IV</td>
<td>18%</td>
</tr>
</tbody>
</table>

(2) Berek JS & Hacker NF, 2000
(3) National Cancer Institute, SEER Data Base 1988-2001
UKCTOCS
(UK Collaborative Trial of Ovarian Cancer Screening)

Inclusion
- Postmenopausal
  - 50 – 74y
  \((n = 202,638)\)

No screening
\((n = 101,359)\)

Annual screening

CA 125
(US as second line)
“MMS”
(multimodal screening)
\((n = 50,640)\)

Transvaginal US
“USS”
\((n = 50,639)\)

<table>
<thead>
<tr>
<th>Type</th>
<th>Count</th>
<th>Incidence/10,000</th>
<th>Stage I/II %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive CA*</td>
<td>58</td>
<td>6 / 10,000</td>
<td>48.3%</td>
</tr>
<tr>
<td>Borderline</td>
<td>28</td>
<td>3 / 10,000</td>
<td></td>
</tr>
</tbody>
</table>

* 48.3% stage I/II

# UKCTOCS
(UK Collaborative Trial of Ovarian Cancer Screening)

<table>
<thead>
<tr>
<th></th>
<th>MMS</th>
<th>USS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repeat test</td>
<td>8.7%</td>
<td>12.0%</td>
</tr>
<tr>
<td>Clinical evaluation</td>
<td>0.3%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Surgery</td>
<td>0.2% (n = 97)</td>
<td>1.8% (n = 845)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>MMS (n = 50,078)</th>
<th>USS (n = 48,230)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA (n)</td>
<td>42</td>
<td>45</td>
</tr>
<tr>
<td>Borderline (n)</td>
<td>8</td>
<td>20</td>
</tr>
<tr>
<td>CA &lt; 1y (n)</td>
<td>5</td>
<td>8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th><strong>MMS</strong></th>
<th><strong>USS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For all CA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>89.4</td>
<td>84.9</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.8</td>
<td>98.2</td>
</tr>
<tr>
<td>PPV</td>
<td>43.3</td>
<td>5.3</td>
</tr>
</tbody>
</table>

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<tr>
<th></th>
<th><strong>MMS</strong></th>
<th><strong>USS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For invasive CA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>89.5</td>
<td>75.0</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.8</td>
<td>98.2</td>
</tr>
<tr>
<td>PPV</td>
<td>35.1</td>
<td>2.8</td>
</tr>
</tbody>
</table>

Screening? NO!
Pelvic pain
Uterine bleeding
Pelvic prolapse
Obesity
Dysuria
Perimenopausal functional scan
Preoperative scan
Dyspareunia
Mesh complications
CAT-scan finding
Incidental findings at pelvic ultrasound after menopause

- Uterus
  - “Thick” endometrium
  - “Polyp”
  - “Fibroid”
- Ovaries
  - Adnexal “mass”
- Other findings
**Incidental** findings at pelvic ultrasound after menopause:

**“Thick”** endometrium

How thick is too thick?

in postmenopausal women **without** vaginal bleeding.

<table>
<thead>
<tr>
<th></th>
<th>ET</th>
<th>Risk of cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>&gt; 5 mm</td>
<td>7.3%</td>
</tr>
<tr>
<td></td>
<td>≤ 5 mm</td>
<td>0.07%</td>
</tr>
<tr>
<td>NO bleeding</td>
<td>&gt; 11 mm</td>
<td>6.7%</td>
</tr>
<tr>
<td></td>
<td>≤ 11 mm</td>
<td>&lt; 0.002%</td>
</tr>
</tbody>
</table>

= based on a **theoretical** cohort

Term, definitions and measurements to describe the sonographic features of the endometrium and intrauterine lesions: a consensus opinion from the International Endometrium Tumor Analysis (IETA) Group.


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Incidental findings at pelvic ultrasound after menopause: tamoxifen

- Endometrial “thickness” …(1)
- Ultrasound PRIOR start tamoxifen(2)
- Fluid instillation sonography!(1,3)

(1) Fung et al Gynecol Oncol 2003 ;91 :154-9
(2) Berlière M et al. Obstet Gynecol 1998 ;91 :40-4
(3) Van den Bosch et al. Ultrasound Obstet Gynecol 2009;34:711-4
Incidental findings at pelvic ultrasound after menopause: “Polyp”

Incidence → 13% - 17%\(^{(1,2,3)}\)

How often malignant in asymptomatic postmenopausal women?

→ Ferrazzi et al.\(^{(4)}\) ~ size

<table>
<thead>
<tr>
<th></th>
<th>Asymptomatic</th>
<th>PMB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>0.1%</td>
<td>1%</td>
</tr>
<tr>
<td>Atypical hyperplasia</td>
<td>1.2%</td>
<td>2.2%</td>
</tr>
</tbody>
</table>

(3) Dreisler E et al. Ultrasound Obstet Gynecol 2009;33:102-8
Incidental findings at pelvic ultrasound after menopause: “Fibroid”

Prevalence at age 50 ~ 50% (1)

→ Why treat it? “if it ain’t broken, don’t fix it!”
  → Treat it before they grow (and become symptomatic)??...
  → It may be a sarcoma!

Incidental findings at pelvic ultrasound after menopause:

**Fibroid or Sarcoma**

SARCOMA

- **cumulative risk**$^{(1)}$ ~ 5 / 10 000
- **prognosis**

<table>
<thead>
<tr>
<th>Tumor confined to the uterus</th>
<th>5-year survival$^{(2)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50%</td>
</tr>
<tr>
<td>Spread beyond the uterus</td>
<td>20%</td>
</tr>
</tbody>
</table>

→ Ultrasound screening for sarcoma ??

(2) Berek JS & Hacker NF, 2000.
Ultrasound features of uterine leiomyosarcomas

- Large
- Oval-shaped
- Inhomogeneous
  - “bizarre” internal echo pattern
  - Central necrosis
- Color imaging
  - Irregular vessel distribution
  - Low impedance
  - High velocities
- Absence of calcifications

**BUT**

much overlap

**NO pathognomonic features**

Simulation

Screening for sarcoma

N = 20,000

SCREENING

Hysterectomy for fibroids
N = 10,000

- 15 deaths

Hysterectomy for sarcoma
N = 5

- 2 – 3 deaths

Missed Sarcoma
N = 5

- 3 – 4 deaths

N = 20,000

NO screening

Sarcoma
N = 10

- 5 – 8 deaths

“collateral damage”

~ 10 – 14 deaths

Incidental findings at pelvic ultrasound after menopause: Adnexal "Mass"

Benign or Malignant?
Adnexal masses: the “obvious” cases

- Serous papillary carcinoma
- Clear cell carcinoma
Adnexal masses: the “less obvious” cases

- **Endometrioma**
- **Benign serous cystadenofibroma**
- **Clear cell cystadenocarcinoma**
Risk of Malignancy Index (RMI)

\[ \text{RMI} = U \times M \times \text{serum CA 125} \]

- **U**: ultrasound score
  - Multilocular cysts
  - Evidence of solid areas
  - Evidence of metastases
  - Presence of ascites
  - Bilateral lesions

  - None of the features = 0
  - 1 feature present = 1
  - > 1 features = 3

- **M**: menopausal status
  - Premenopausal = 1
  - Postmenopausal = 3

The receiver operating characteristic (ROC) curves of the logistic regression model (M1) and ROC of the Risk of Malignancy Index (RMI) and ROC of an old logistic regression model (LR) by Timmerman et al applied to the test set cases with serum CA-125 results available. The areas under the curve (AUC) are 0.94, 0.87, and 0.90, respectively.

Simple ultrasound-based rules for the diagnosis of ovarian cancer.

- Rules for predicting a **malignant** tumor (**M-rules**)
  
  - **M1** Irregular solid tumor
  
  - **M2** Presence of ascites
  
  - **M3** $\geq 4$ papillary structures
  
  - **M4** Irregular multilocular solid tumor with largest diameter $\geq 100$ mm
  
  - **M5** Very strong blood flow (**color score 4**)

If one or more **M-rules apply** in the absence of a **B-rule**, the mass is classified as **malignant**.

Simple ultrasound-based rules for the diagnosis of ovarian cancer.

- **Rules for predicting a **benign** tumor (B-rules)**
  - **B1** Unilocular
  - **B2** Presence of solid components where the largest solid component has a diameter < 7mm
  - **B3** Presence of acoustic shadows
  - **B4** Smooth multilocular tumor with largest diameter < 100 mm
  - **B5** No blood flow (color score 1)

*If one or more B-rules apply in the absence of a M-rule, the mass is classified as **benign**.*

Simple ultrasound-based rules for the diagnosis of ovarian cancer.

If both M-rules and B-rules apply, the mass cannot be classified.

If no rule applies, the mass cannot be classified.

- Rules applicable in 76% of tumors
- Sensitivity 95%
- Specificity 91%
- LR+ 10.37
- LR - 0.06

Incidental findings at pelvic ultrasound after menopause:

- ascites

DD/
- Ovarian cancer
- Cirrhosis
- Dialysis
- Ventriculo-peritoneal drain
- ...
Incidental findings at pelvic ultrasound after menopause:

- papillary structures
- hydrosalpinx
Incidental findings at pelvic ultrasound after menopause:

Other findings

- Age: 75 years old
- Reports irregular vaginal bleeding (spotting) since 36 months
- Ultrasound of the uterus: thin & regular endometrium

Bladder cancer

Incidental findings at pelvic ultrasound after menopause:

Other findings

- Age: 86 years old
- History of hysterectomy for myoma
- Presents with vaginal bleeding and dysuria
Transverse section

Vaginal lymphoma

Pipelle aspiration
Incidental findings at pelvic ultrasound after menopause:

Other findings

- Age: 54 years old
- Menopause at 44y
- Heavy smoker
- Postmenopausal bleeding since > 1 year

Cervical cancer
Incidental findings at pelvic ultrasound after menopause:

Other findings

- Age: 80 years old
- Reports
  - Irregular vaginal bleeding (spotting) for 1 year, especially after passing urine
  - Lower abdominal pain
- Ultrasound of the uterus: thin & regular endometrium
*Incidental* findings at pelvic ultrasound after menopause:

Other findings

**Diverticulitis involving the posterior bladder wall**
Use of pelvic ultrasound screening in postmenopausal women

Conclusions

Screening? No

Incidental findings
- avoid “overtreatment”
- “good clinical judgement”
Pelvic ultrasound after menopause

- “primum non nocere”!

- Need for more studies in the asymptomatic population!