# Kohdunrunkosyöpä

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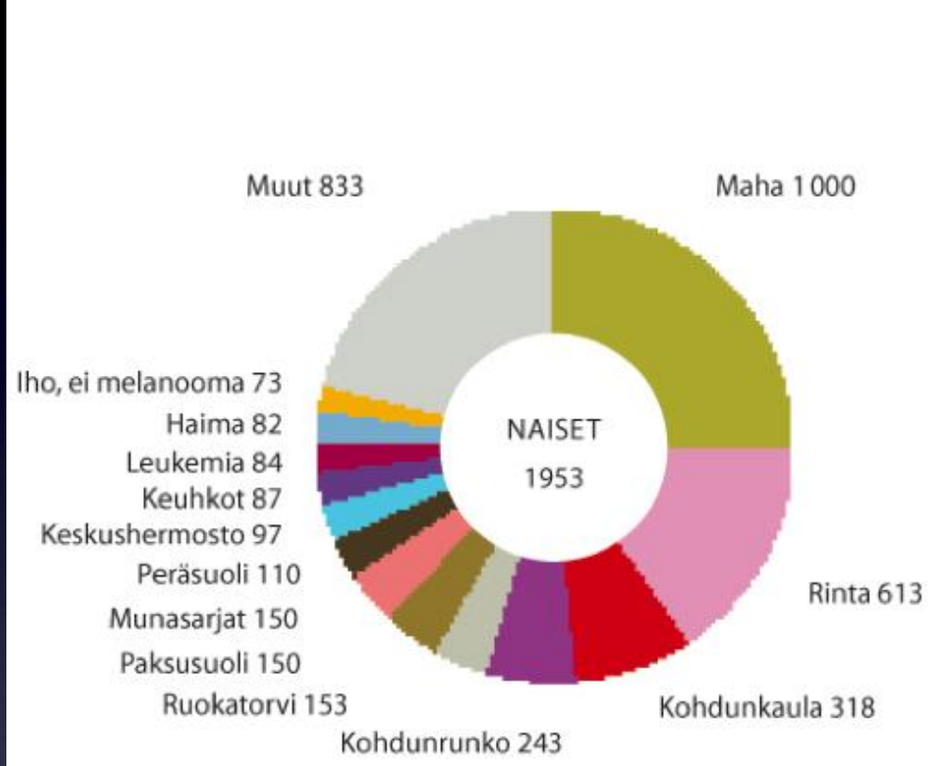
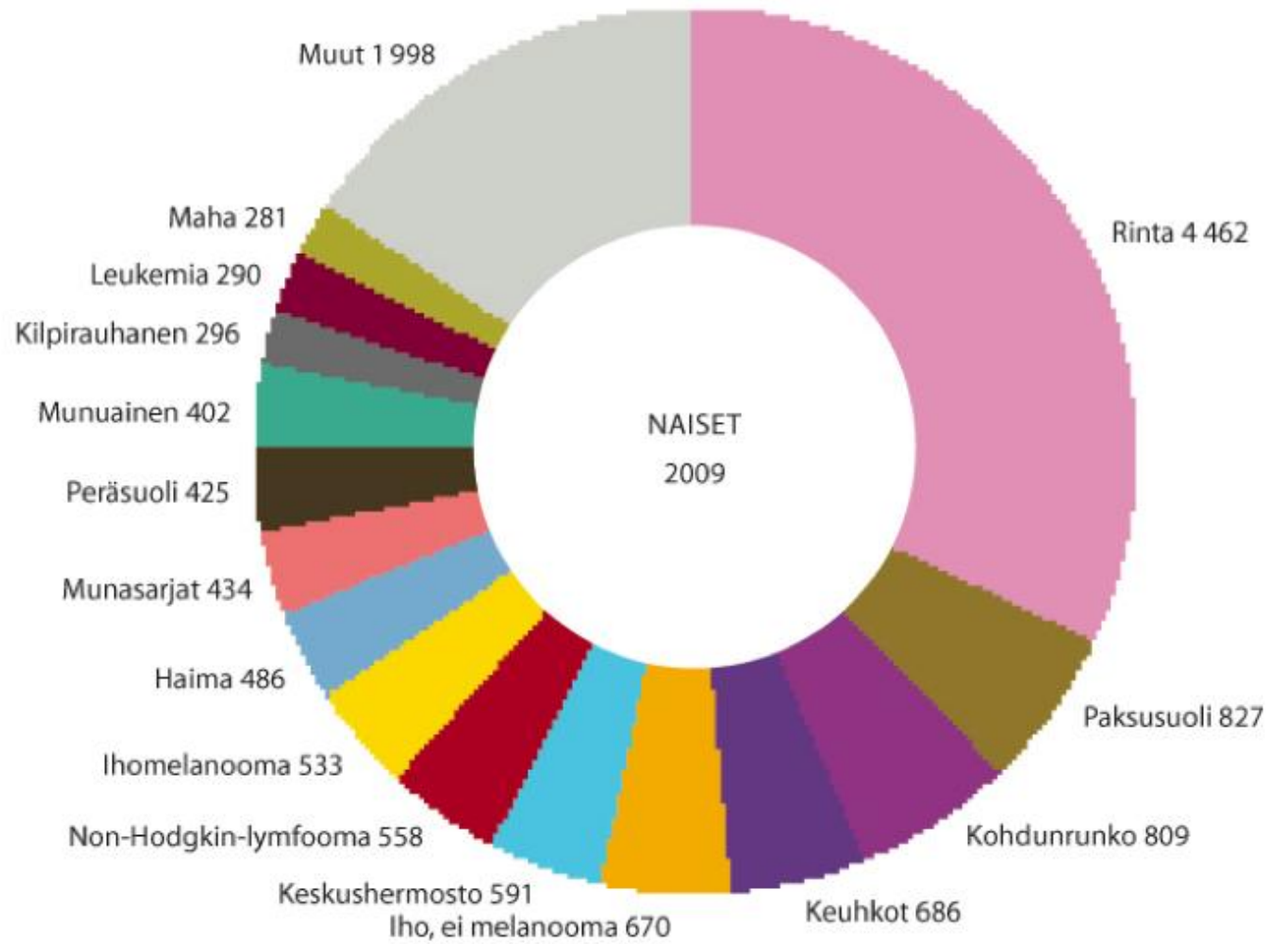
EGO/ONKOLOGIA 18.10.2012

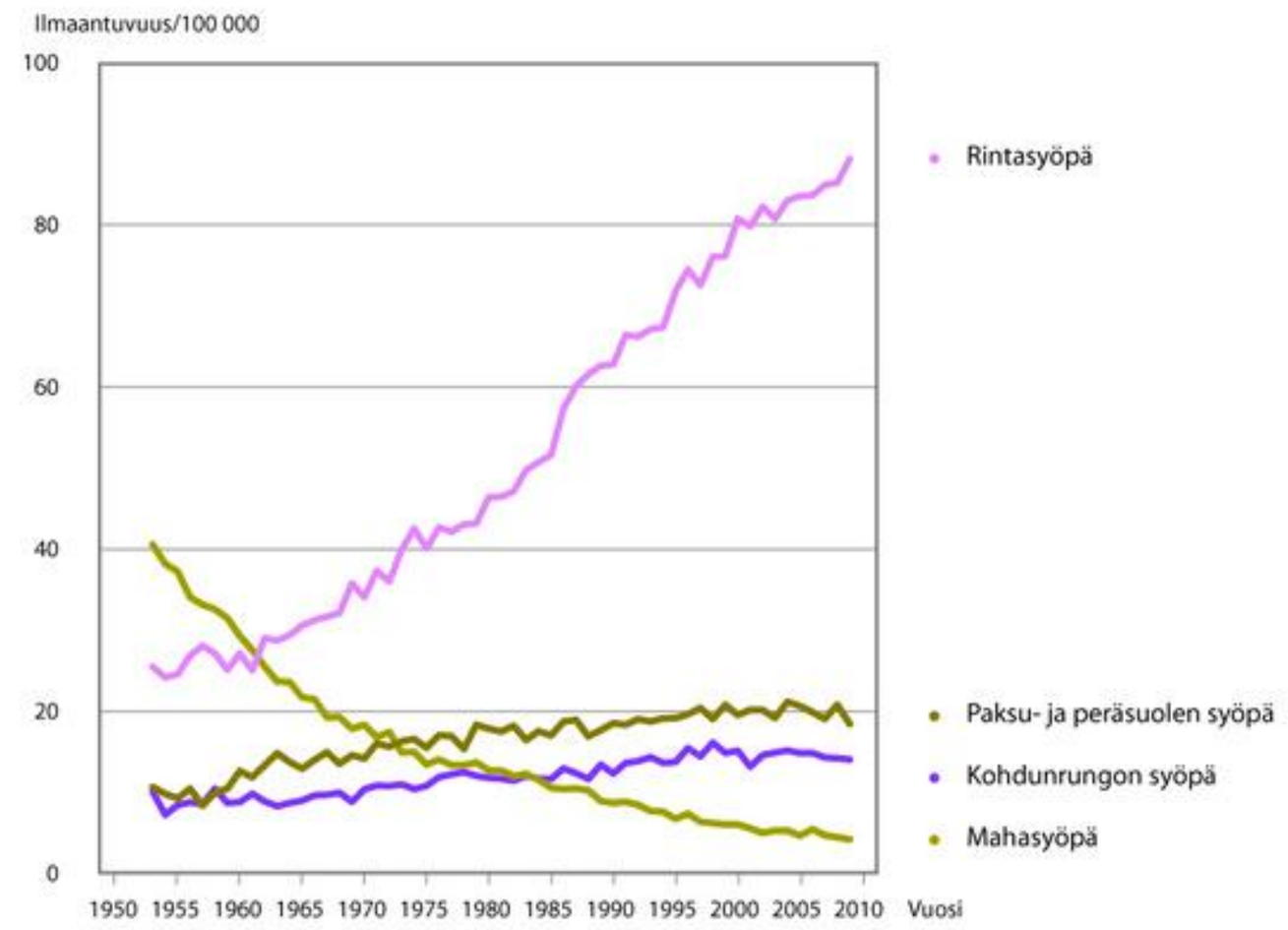
Naisten uusien syöpätapausten määrät vuosina 1953 ja 2009.
Ympyrän pinta-ala kuvaa syöpien kokonaismäärän muutosta.




# Muutos naisten syövissä 55 vuodessa Suomessa

Yleisimpien syöpien ikävakioitu ilmaantuvuus Suomessa vuosina 1953–2009.




*Pukkala E, Sankila R, Ranualahti M.*
*Syöpä Suomessa 2011*
*Suomen Syöpäyhdistyksen julkaisuja nro 82.*

# Naisten syöpien ilmaantuvvus 1950-2009

# Maailmanlaajuisesti yleisin gynekologinen syöpä

Suomessa vuonna 2010

804 tapausta

%-osuus 5.6

ilmaantuvuus13.5/ 100 000

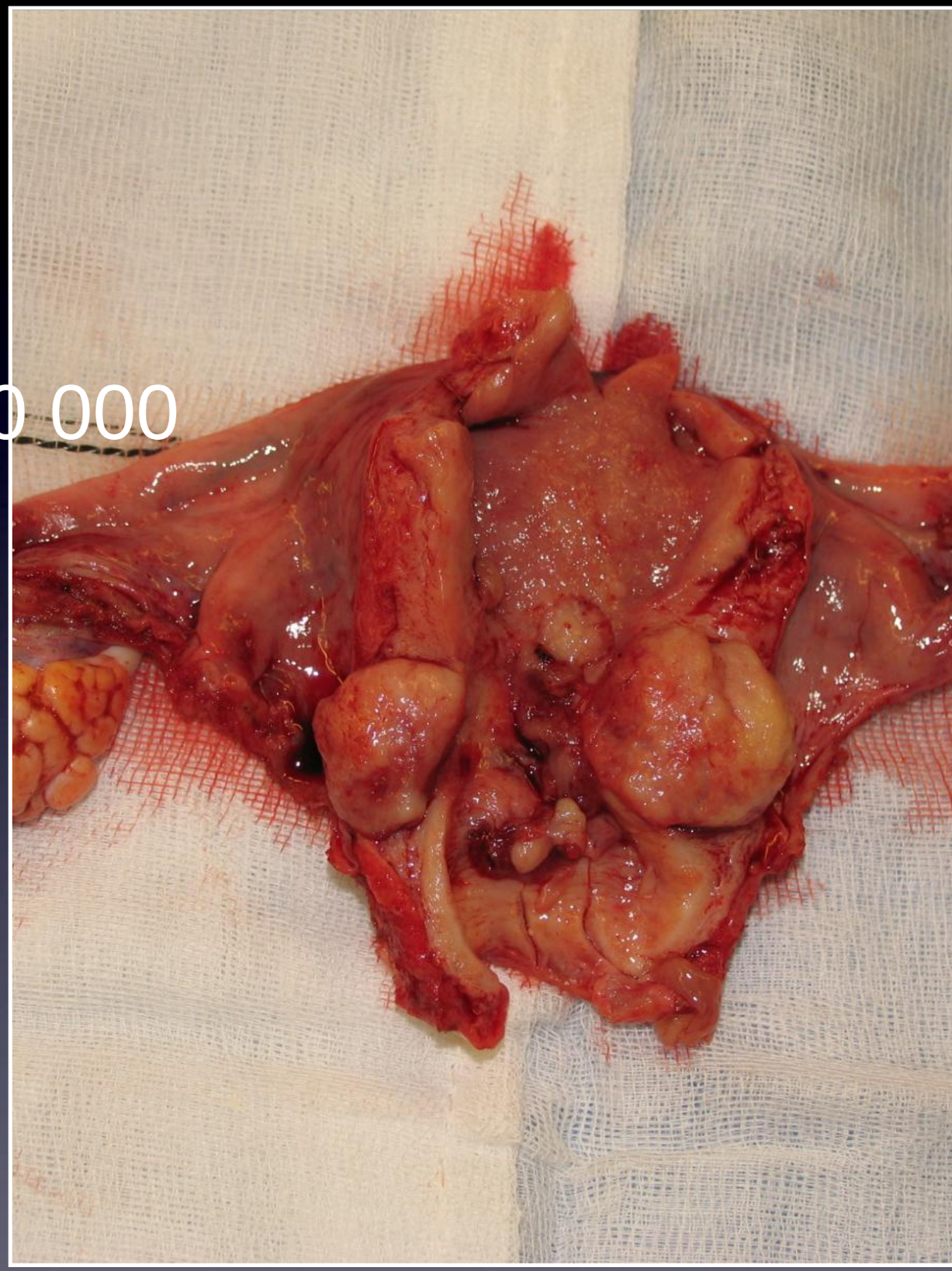
Elinikäinen riski (USA) 2.6%

Esiintymishuippuikä 60+

alle 45 vuotialla 5-30%

1.6% 20-34 vuotialla

6.1% 35-44 vuotialla



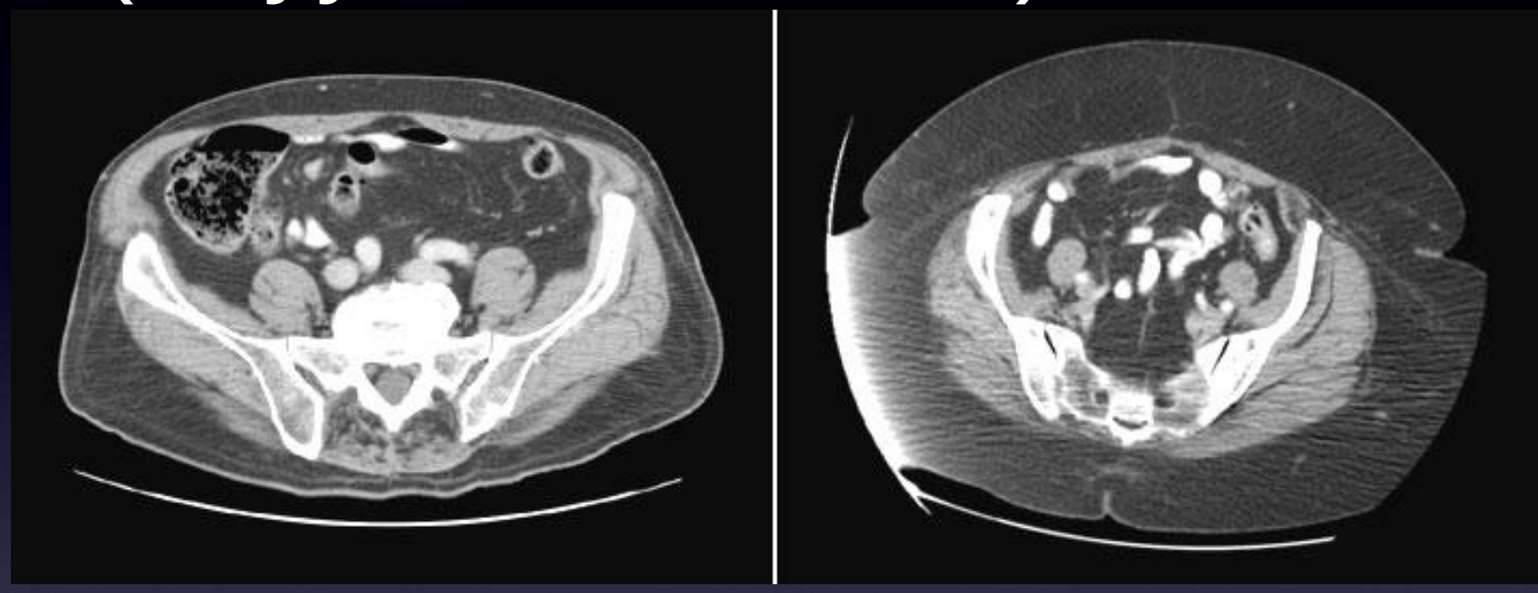
http://seer.cancer.gov/faststats.

- Sarkoomat:
  - Kohdun lihaksesta
    - leiomyosarkoomat
- Endometrium karsinoomat EC:
  - Kohdun limakalvon rauhasista
    - endometrioidinen adenocarcinoma 90%
    - papillaarinen seroosi karsinooma
    - clear-cell (kirkassoluinen) karsinooma
- Endometriumin strooma sarkoomat
  - Endometriumin sidekudoksesta
- Malignit Müllerian tiehyt kasvaimet
- Karsinosarkooma käyttäytyy kuten huonosti erilaistunut karsinooma

# Sarkoomat 2-5% kohdun maligniteeteista

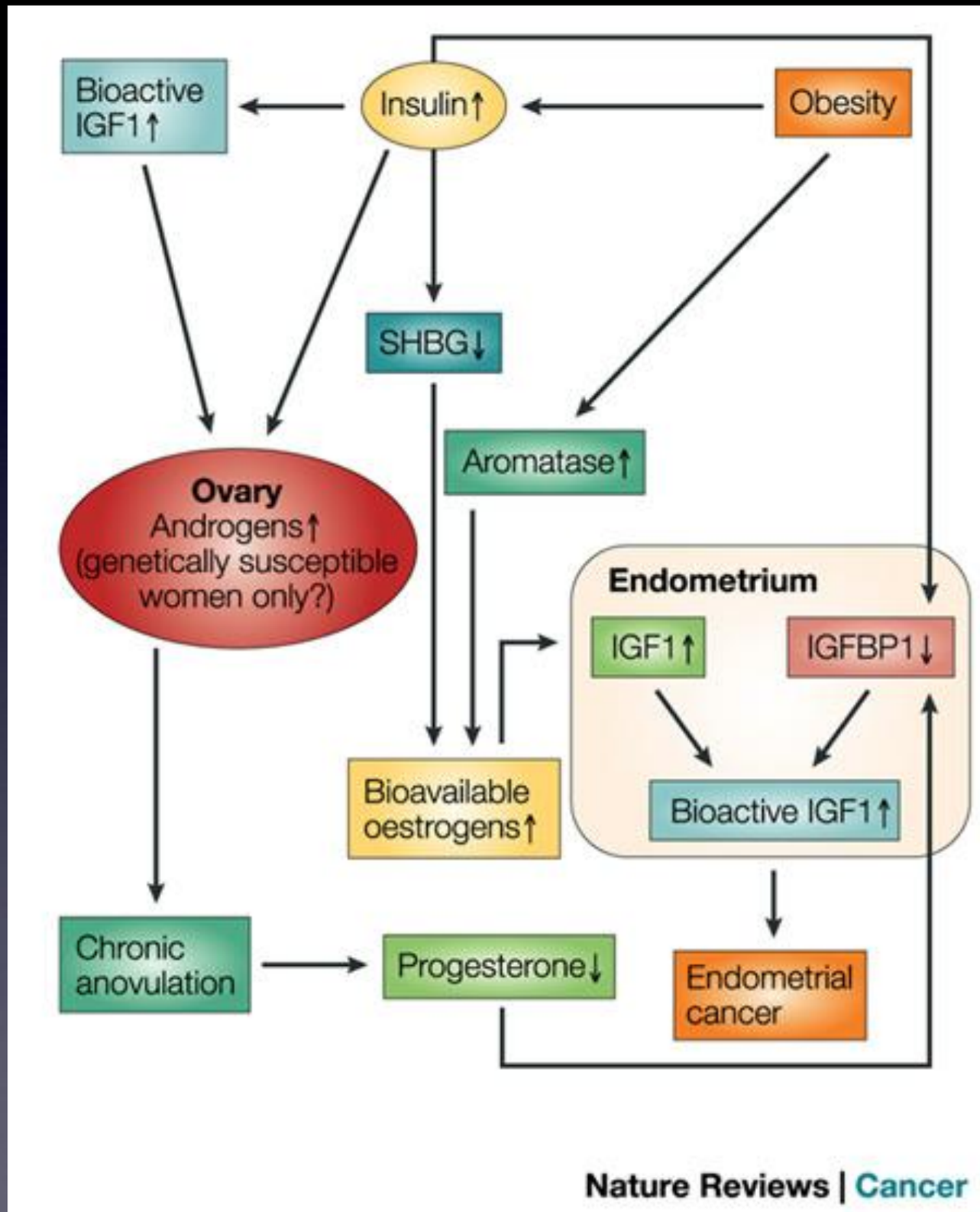
- Karsinosarcoma 40% - 50% sarkoomista
- Leiomyosarkooma (myometrium)
  - esiintymishuippu 50 vuotta
  - 30% sarkoomista
- Endometriumin strooma sarkoomat 15% sarkoomista
- Altistus: sädetys, tamoksifeeni

- Obesiteetti----jos paino >23kg yli normaalin, riski 10x
- Synnyttämättömyys (liittyy infertiliteettiin) RR 2.0
- DM RR 2.7
- PCO
- Tamoksifeeni



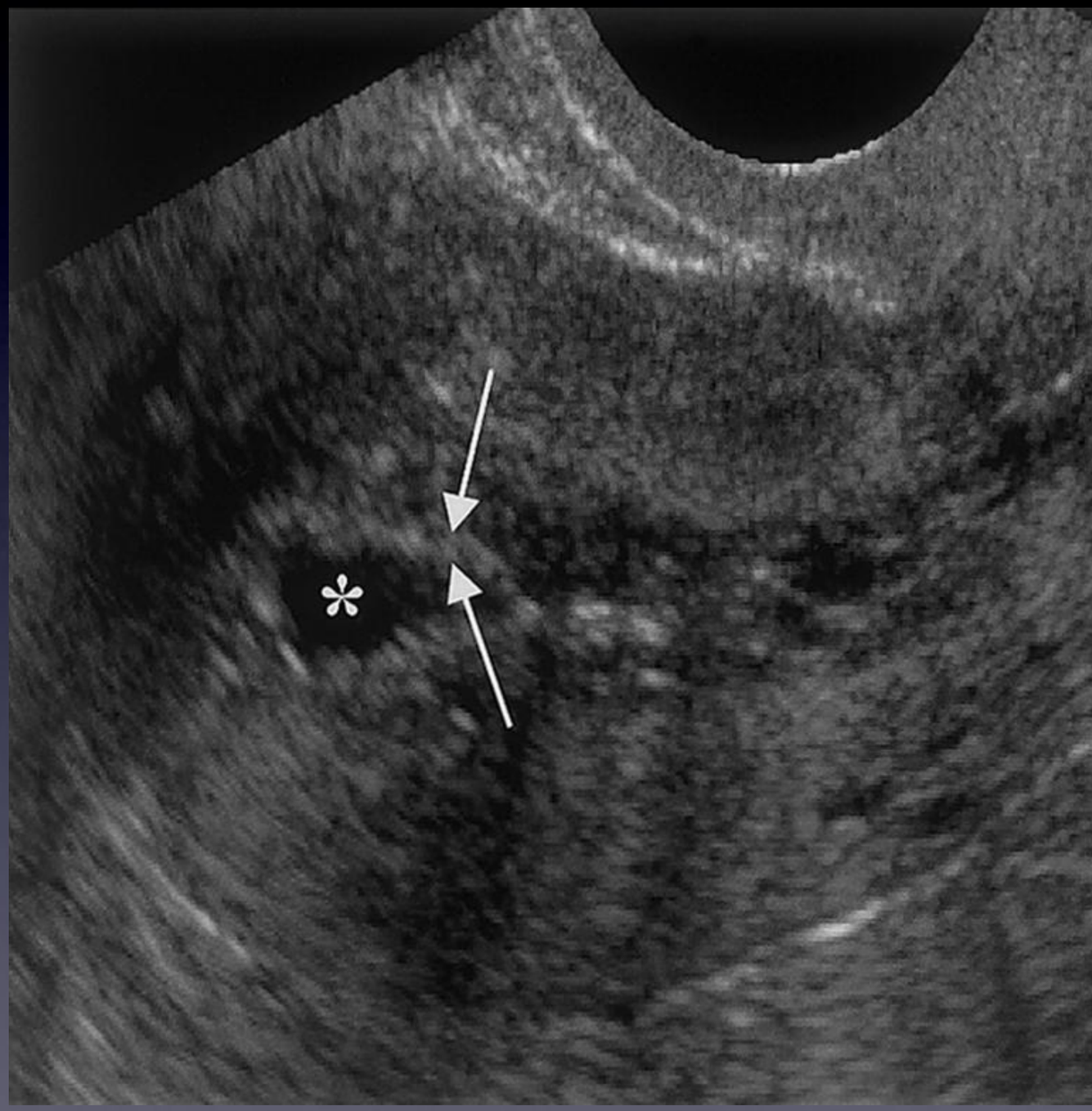
- Estrogeeni, jos prog annos ei ole riittävä RR 4-8, kesto 10 vuotta
- Atyyppinen adenomatoottinen hpl RR 8-28
- Hereditaarinen Non-Polypoottinen Colorektaalinen Cancer (HNPCC) ---40–60% elinikäinen EC riski

# Obesiteetin vaikutus EC:ssa

# Tamoksifeeni

- Subepiteliaalinen strooman hypertrofia
- Endometriumin paksuus ei kerro maligniteettiriskistä
  - ei rutiinisti UÄ
- Jos veristä vuotoa, syyn selvittäminen: UÄ, Pipelle



# Endometriumin hyperplasia

- simple or complex
  - without or with cytological atypia.

- Simple hyperplasia often spontaneously regresses and rarely progresses to endometrial cancer

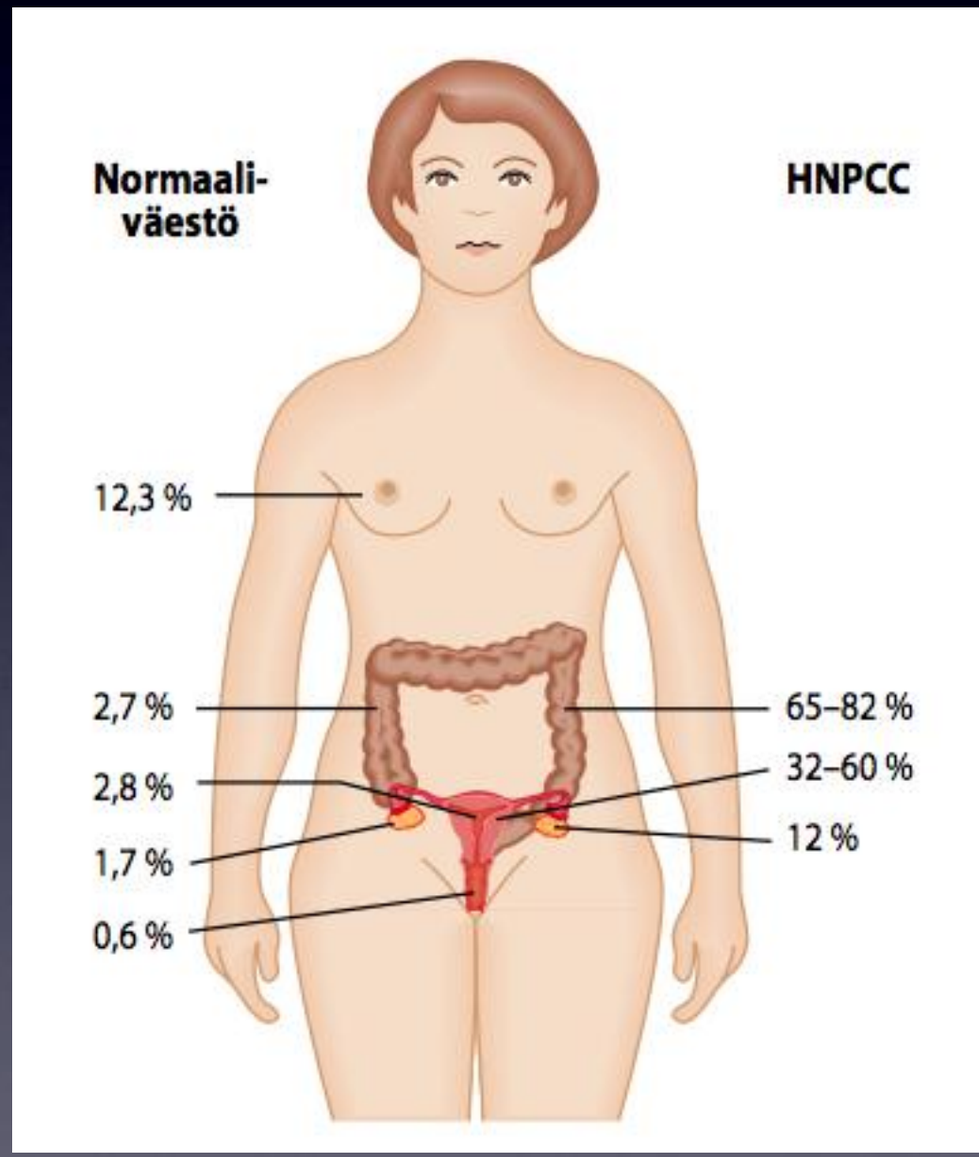
- Complex hyperplasia and atypical hyperplasia, in particular, are more likely to progress to cancer and are therefore commonly treated

- Simple hyperplasia without atypia – (1 %)
- Complex hyperplasia without atypia – (3 %)
- Simple atypical hyperplasia – (8 %)
- Complex atypical hyperplasia – (29 %)

Kurman RJ. The behavior of endometrial hyperplasia. A long-term study of "untreated" hyperplasia in 170 patients. Cancer. 1985;56(2):403

# HNPCC

- periytyy vallitsevasti
- kolorektaalisyövän lisäksi usein myös muita syöpiä, tyypillisesti endometrium-, munasarja- sekä mahasyöpää
- HNPCC aiheutuu suomalaissuvuissa pääasiassa MLH1-geenin mutaatioista, harvemmin MSH2- tai MSH6-geenien mutaatioista.




Leminen A Duodecim 2006

# EC suojatekijät

- Tilat, joissa estrogeenitasot matalat
  - tupakointi
  - E-pillerit
    - 40% jopa 15 vuotta lopettamisen jälkeen
    - Riskin väheneminen korreloi käyttöaikaan: 4v---->56%, 8 ----->67%, 12v----->72%

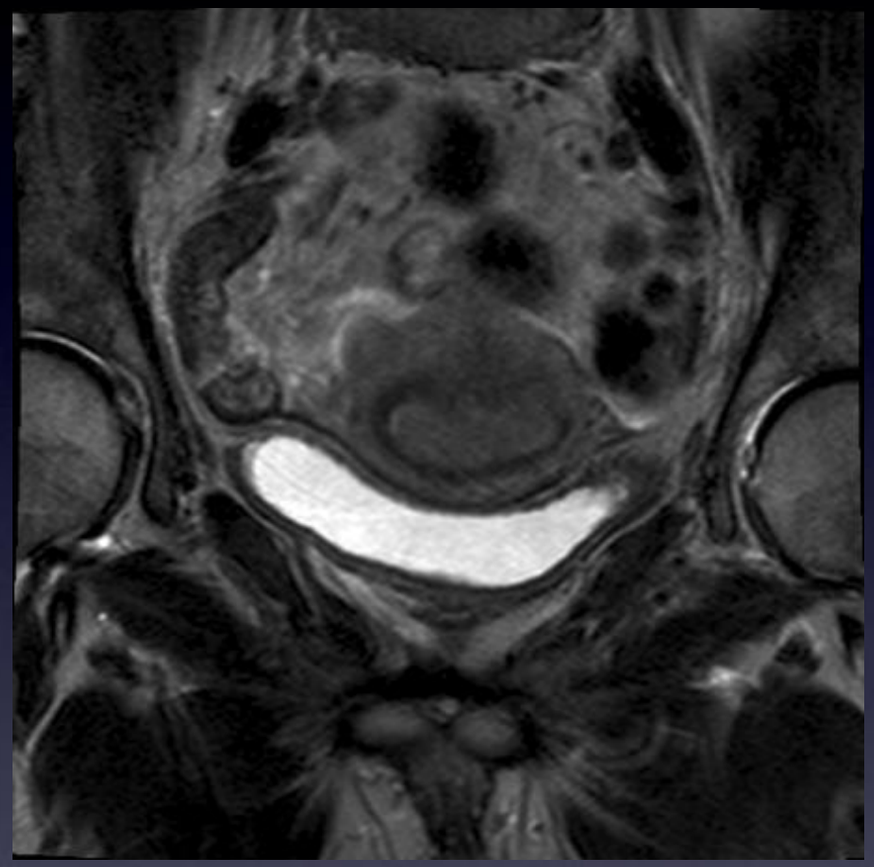
# EC oireet

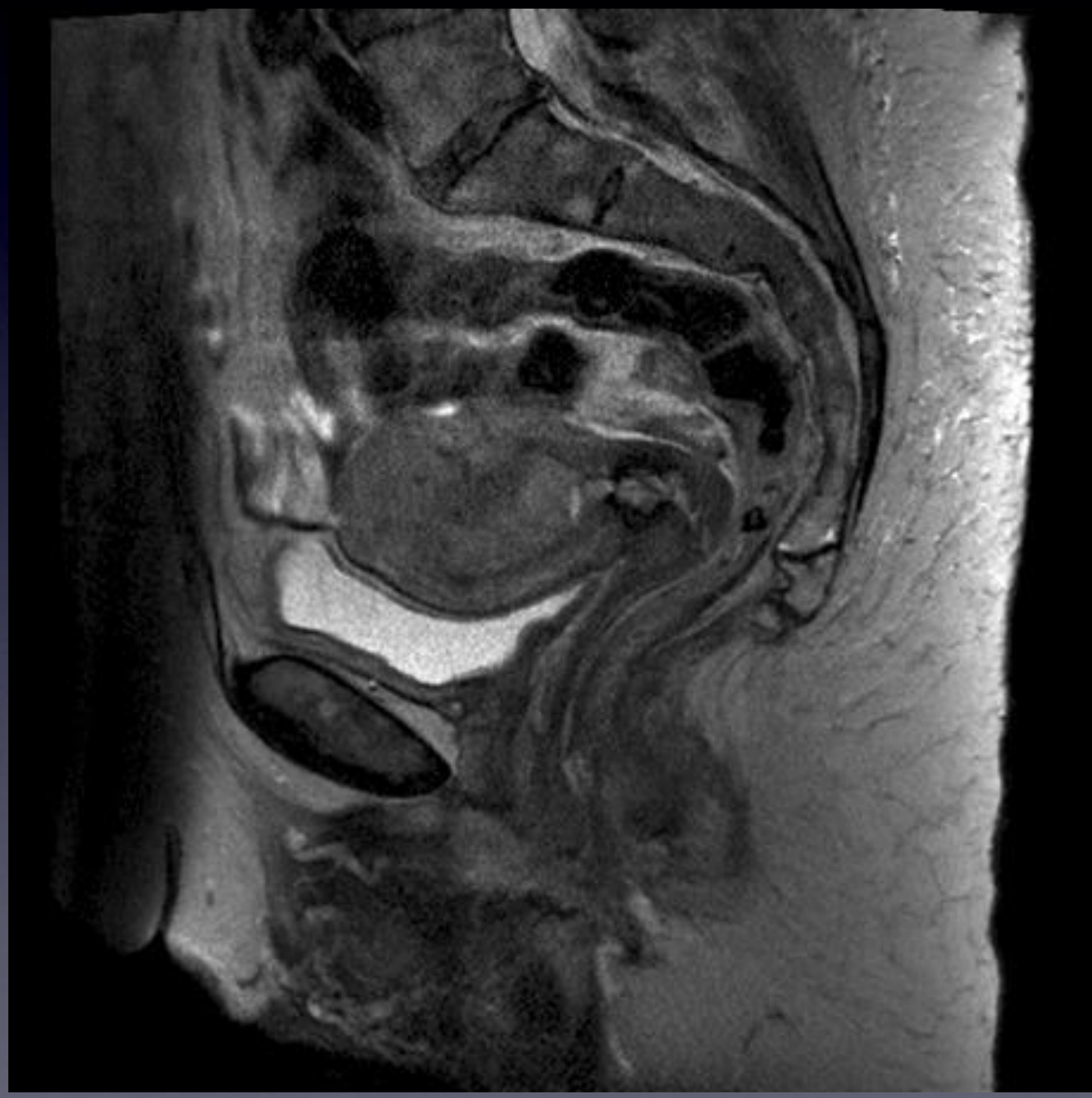
- Postmenopausaalinen (PM) vuoto
  - syy 7% ca, 56% atrofia, 15% hyperplasia
  - ca todennäköisyys PM-vuodon syynä kasvaa iän myötä
    - 16% 60-vuotialla, 60% 80-vuotialla
- 20% diagnostisoidaan ennen PM
  - PAPA atyyppiset lieriösolut, 23% ca
  - PAPA löytää n 50% EC
  - Pipelle vuotohäiriöt, erityisesti riskiryhmät

# Tutkimukset

- Histologia
  - Pipelle, kaavinta, HYS+biopsia,
  - SIS
  - Kuvantaminen
    - THX, UÄ, MRI

# MRI





- Invaasion syvyys
- Imusolmukkeet

# Kohdun limakalvon karsinogeneesi tyyppi I ja II

| | | | |
|---|---|---|---|
| I | Simplex/ Complex Hyperplasia | Atyyppinen Hyperplasia | Endometrioidi 75-85% G1, G2,(G3) -adenopapillaarinen -villoglandulaarinen |
| Normaali | | | |
| II | | | Endometrioidi G3<br>-seröösi<br>-clear cell |

**The most frequent early molecular genetic alterations in type I tumors are**

- **-mutations in the PTEN tumor suppressive gene**
- **-K-ras oncogene**
- **-microsatellite instability**

**Type II tumors are more often associated with p53 mutations**

**Table 1: 2009 FIGO staging system for carcinoma of the endometrium**

| | | | |
|---|---|---|---|
| Stage I[a] | Tumor contained to the corpus uteri | | |
| | IA | | No or less than half myometrial invasion |
| | IB | | Invasion equal to or more than half of the myometrium |
| Stage II | | | Tumor invades the cervical stroma but does not extend beyond the uterus[b] |
| Stage III[a] | | | Local and/or regional spread of tumor[c] |
| | IIIA | | Tumor invades the serosa of the corpus uteri and/or adnexas |
| | IIIB | | Vaginal and/or parametrial involvement |
| | IIIC | | Metastases to pelvis and/or para-aortic lymph nodes |
| | | IIIC1 | Positive pelvic nodes |
| | | IIIC2 | Positive para-aortic lymph nodes with or without positive pelvic lymph nodes |
| Stage IV[a] | | | Tumor invades bladder and/or bowel mucosa and/or distant metastases |
| | IVA | | Tumor invasion of bladder and/or bowel mucosa |
| | IVB | | Disant metastases, including intra-abdominal metastases and or inguinal lymph nodes |

FIGO = International Federation of Gynecology and Obstetrics

[a] Includes grades 1, 2, or 3

[b] Endocervical glandular involvement only should be considered as stage I and no longer as stage II.

[c] Positive cytology has to be reported separately without changing the stage.

# Fertiliteetin säästäminen

## EC

- 8-14% potilaista fertiili-iässä
- syöpäsolujen hormonireseptori -status
- responssi 26-89% ER+ PR+
- responssi 8-17% ER-PR-

gradus 1
LVSI negat
ei myometrium invaasiota MRI
ei metastaaseja CT
ei adnex tuumoria CT tai UÄ
29% CC OVCA
PR-reseptorit++/+++

# HPL tai EC ja fertiliteetin säästäminen



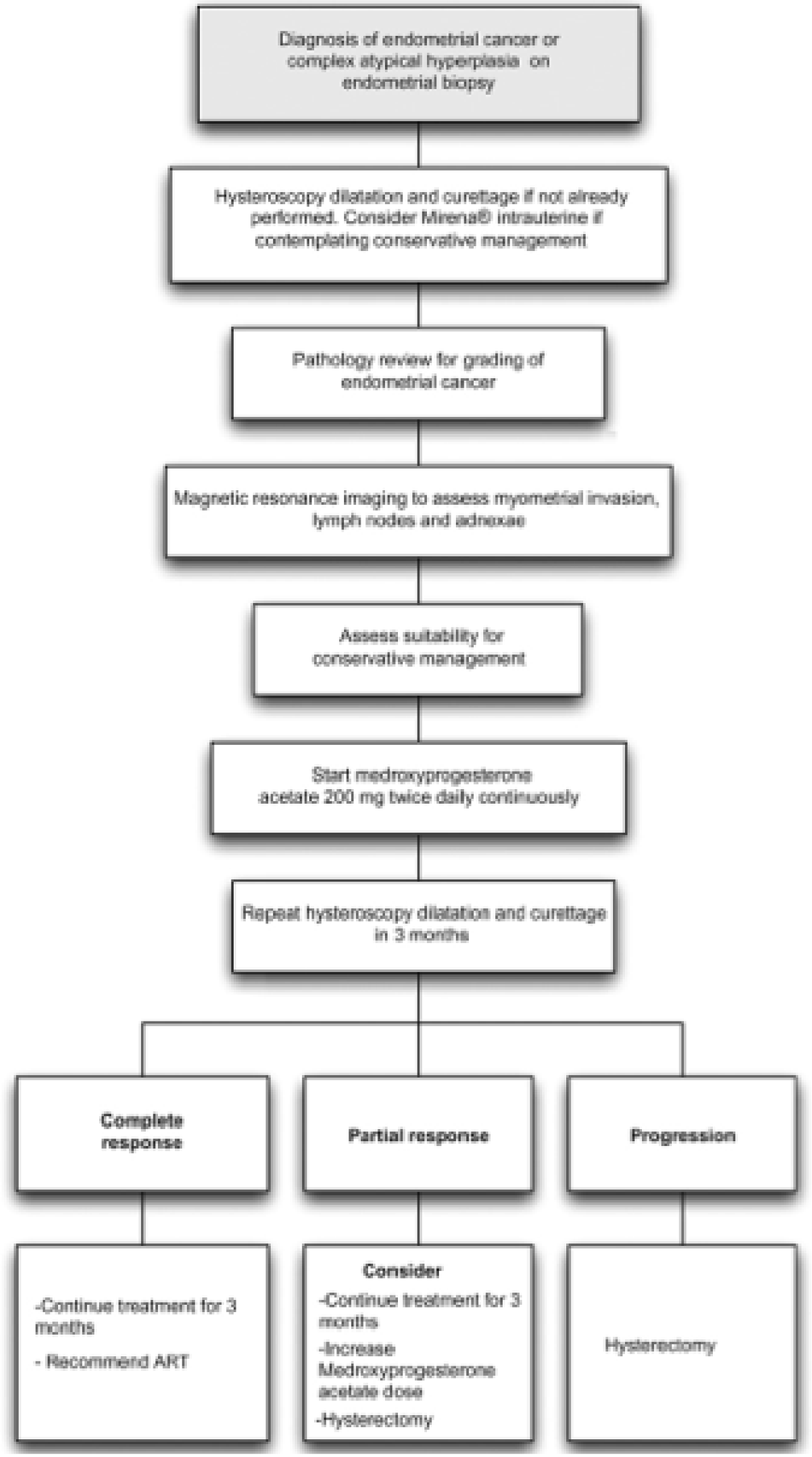



**Fig. 2.** Recommended algorithm for conservative management of endometrial cancer in young women.

TABLE 5

**Regression, relapse and obstetric outcomes in women with endometrial cancer treated conservatively with progestin therapy**

| Author | Patients | Regression | Relapse | Live births | Progesterone |
|---|---|---|---|---|---|
| Randall and Kurman[83] | 12 | 9 | 1 | 6 | Megestrol or MPA |
| Duska et al[84] | 12 | 10 | 1 | 5 | MPA |
| Imai et al[85] | 14 | 8 | 3 | 3 | MPA |
| Kaku et al[86] | 12 | 9 | 2 | 1 | MPA |
| Wang et al[87] | 9 | 8 | 4 | 3 | Megestrol |
| Niwa et al[88] | 12 | 12 | 8 | 5 | MPA |
| Lowe et al[89] | 2 | 2 | 0 | 8 | Megestrol |
| Sardi et al[90] | 4 | 3 | 0 | 3 | MPA |
| Yang et al[91] | 6 | 4 | 2 | 2 | Megestrol |
| Farhi et al[77] | 4 | 3 | 1 | 2 | Progestin |
| Gotlieb et al[92] | 13 | 13 | 6 | 9 | Megestrol |
| Total | 100 | 81 (81%) | 28 (28%) | 47 (47%) | |

*MPA*, medroxyprogesterone acetate.

*Eskander. Fertility preservation in patients with gynecologic malignancies. Am J Obstet Gynecol 2011.*

# Tuloksia

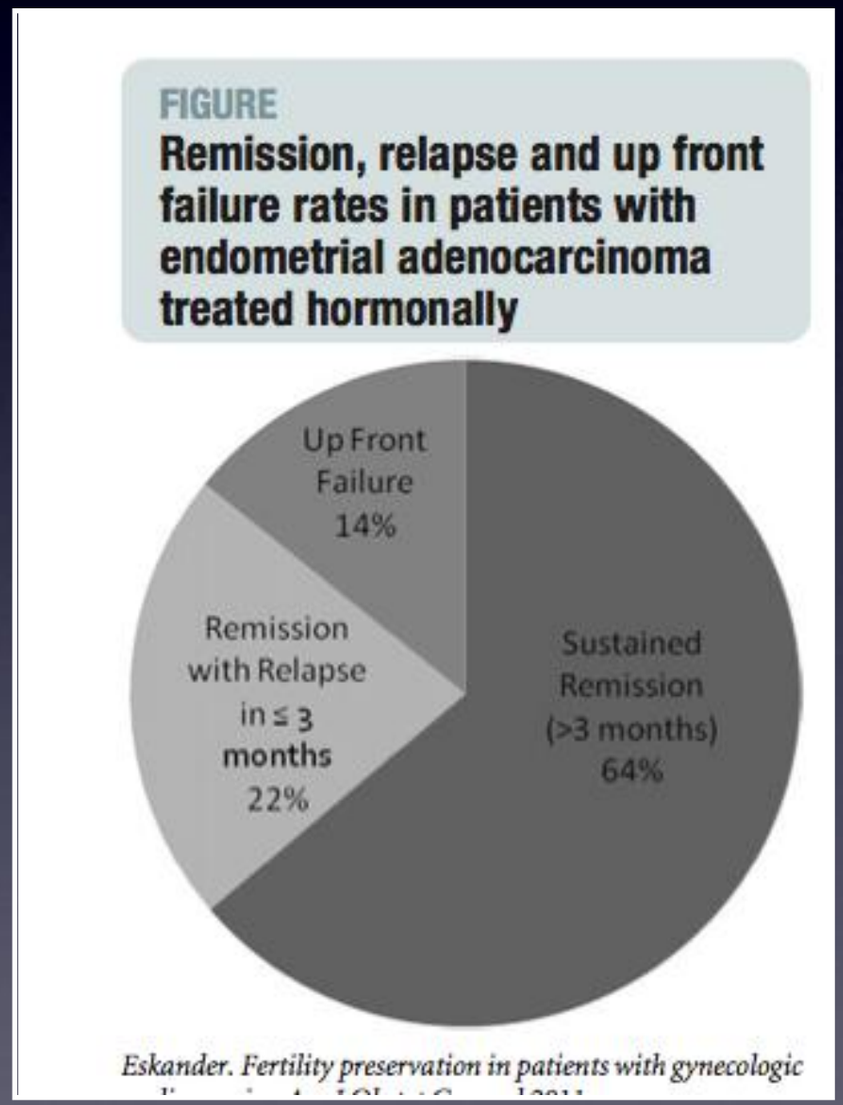
# Tulokset EC ja säästävä hoito

- Huolellinen neuvonta, mikäli nuorelle naiselle tarjotaan ei-standardi hoitoa

- Onkologinen, geneettinen, hedelmällisyys ja psykologinen neuvonta

- Moniammatillinen osaaminen

  - gyn. onkologia, obstetriikka, reproduktio endokrinologia, radiologia, patologia



# Riskiluokitus
# Imusolmuke metastasoinnin riski

LN RISKI
<5%

LN RISKI
Pelvic 5-9%
PA 4%

LN RISKI
Pelvic 60-80%
PA 10-30%

| Low Risk | Intermediate Risk | High Risk |
|---|---|---|
| Stage IA, grade 1 or 2 (histological type 1) | Stage IA, grade 3 (histological type 1)<br>Stage IB, grade 1 or 2 (histological type 1) | Stage IB, grade 3 (histological type 1)<br>Stage IA–B (histological type 2)<br>Stage I with lymphovascular space invasion* |

*Addition to ESMO guidelines (stage IA: tumor confined to the corpus uteri [no or <50% of the myometrium]; stage IB: tumor confined to the corpus uteri [invasion ≥50% of the myometrium]).

Clinical practice guidelines for the management of patients with endometrial cancer in France: recommendations of the Institut National du Cancer and the Societe Francaise d'Oncologie Gynecologique.
Querleu D; Planchamp F; Narducci F; Morice P; Joly F; Genestie C; Haie-Meder C; Thomas L; Quenel-Tueux N; Darai E; Dorangeon PH; Marret H; Taieb S; Mazeau-Woynar V; Institut National du Cancer; Societe Francaise dOncologie Gynecologique

International Journal of Gynecological Cancer. 21(5):945-50, 2011 Jul.

Table. No caption available.

# European Society for Medical Oncology GUIDELINE

| | | |
|---|---|---|
| Stage I | IA G1–G2 | Hysterectomy with bilateral salpingo-oophorectomy |
| | IA G3 | Hysterectomy with bilateral salpingo-oophorectomy ± bilateral pelvic/para aortic lymphadenectomy |
| | IB G1 G2 G3 | Hysterectomy with bilateral salpingo-oophorectomy ± bilateral pelvic/para aortic lymphadenectomy |
| Stage II | | Hysterectomy with bilateral salpingo-oophorectomy and bilateral pelvic/par aortic lymphadenectomy |
| Stage III | | Maximal surgical cytoreduction with a good performance status |
| Stage IV | IVA | Anterior and posterior pelvic exenteration |
| | IVB | Systemic therapeutical approach with palliative surgery |

# ENNUSTE

STAGE
GRADE
INVAASION SYVYYS
LVSI
HISTOLOGINEN TYYPPI

EC Tyyppi I 5VOS 83%
EC Tyyppi II 5VOS 53-65%

# Lymphadenektomia

- LN ongelmat
  - Leikkausaika pitenee, verenvuoto, lymfakystat, lymfaturvotus (1-27%)
  - Lymphödemalle altistavat tekijät: sädehoito, perifeerinen LN, >30 LN


- Kitchener H, Swart AM, Qian Q, et al. Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. Lancet 2009; 373:125–136.
- Benedetti Panici P, Basile S, Maneschi F, et al. Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma:randomized clinical trial. J Natl Cancer Inst 2008; 100:1707–1716.

# TYYPPI I EC
# Matala riski

♦ **Histological type 1**

**LOW RISK**

- TH/BSO is recommended.
- Lymphadenectomy is not recommended.
- *Postoperative high-dose rate BT can be considered if there is a myometrial involvement.*
- EBRT is not recommended.
- *Conservative treatment of the uterus can be considered for patients who wish to become pregnant in the future, who have tumors that are assessed as stage I, grade 1 with no invasion of the myometrium, preferably following laparoscopic exploration of the ovaries to rule out serous disease and disease outside the uterus.*
- *With the same caveats, conservative ovarian treatment can be considered in association with total hysterectomy and bilateral salpingectomy for patients younger than 40 who wish to maintain ovarian function.*
- CT is not recommended.

# Keskikorkea riski EC

## INTERMEDIATE RISK

- TH/BSO is recommended.
- Pelvic lymphadenectomy is not recommended. *However, this can be considered for stage IB grade 2 or stage IA grade 3 with myometrial involvement.*
- The usefulness of detecting a sentinel lymph node in these patients is ongoing.
- Postoperative high-dose rate BT is recommended. EBRT is not recommended.
- CT is not recommended.

# Korkea riski EC

**HIGH RISK**

- TH/BSO is recommended.
- Para-aortic and iliac lymphadenectomy is recommended. Laparoscopic surgery is recommended by extraperitoneal approach, if possible, to reduce the risk of adherences.
- *Pelvic lymphadenectomy can be considered. Its usefulness as a therapy for patients who have no enlarged lymph nodes on imaging and who will receive external radiation to the pelvic area has not been demonstrated.*
- If the hysterectomy operative specimen reveals factors suggestive of a high-risk of recurrence, repeated lymph node and/or peritoneal staging is recommended, preferably by laparoscopy.
- Postoperative pelvic EBRT is recommended.
- *Additional therapy with vaginal BT can be considered.*
- CT is not recommended.

# TYYPPI II

- **Histological type 2**

**CLEAR CELL OR PAPILLARY SEROUS CARCINOMA**

- TH/BSO, pelvic and para-aortic lymphadenectomy, infracolic omentectomy, peritoneal cytology, and biopsies are recommended.

- Postoperative pelvic EBRT is recommended.
- *CT can be considered.*
- *Additional therapy with vaginal BT can be considered.*

# STAGE II

## Tumor Invades Cervical Stroma But Does Not Extend Beyond the Uterus—Stage II

- Hysterectomy with BSO is recommended. Hysterectomy can be simple or enlarged, with or without vaginectomy, depending on the nature of the tumor, with the aim of achieving healthy operating margins.
- Pelvic lymphadenectomy is recommended.
- *For histological type 1, para-aortic lymphadenectomy can be considered, as an initial measure or following pelvic lymphadenectomy if there are positive pelvic lymph nodes.*
- For histological type 2 disease, infracolic omentectomy, pelvic and para-aortic lymphadenectomy, peritoneal cytology, and biopsy are recommended.
- Postoperative EBRT is recommended, in association with postoperative vaginal high-dose rate BT.
- *For histological type 2, adjuvant CT can be considered as a complement to EBRT.*
- *If a large volume of the cervix is affected, preoperative pelvic EBRT with or without preoperative BT can be considered.*

# STAGE III

## Local and/or Regional Spread of the Tumor—Stage III

### TUMOUR INVADES SEROSA OF THE CORPUS UTERI AND/OR ADNEXA—STAGE IIIA

- TH/BSO, infragastric omentectomy, pelvic and para-aortic lymphadenectomy, and peritoneal cytology are recommended.
- If the serosa alone is affected, postoperative pelvic EBRT in association with postoperative high-dose rate BT is recommended.
- If the cervix is affected, postoperative high-dose rate BT is recommended.
- If the adnexa are affected, adjuvant CT is recommended.

# STAGE IV

## Tumor Invades Bladder/Bowel Mucosa and/or Distant Metastases—Stage IV

### TUMOUR INVASION OF BLADDER AND/OR BOWEL MUCOSA—STAGE IVA

- Pelvic EBRT followed by BT is recommended.
- *Concomitant CT can be considered, by analogy with cervical cancer.*
- If radiotherapy fails, pelvic exenteration (curative intent) can be considered.

# Adjuvanttihoito

| | | |
|---|---|---|
| Stage I | IA G1–G2 | Observation |
| | IA G3 | Observation or vaginal brachytherapy |
| | | If negative prognostic factors pelvic radiotherapy and/or adjunctive chemotherapy could be considered |
| | IB G1 G2 | Observation or vaginal brachytherapy |
| | | If negative prognostic factors pelvic radiotherapy and/or adjunctive chemotherapy could be considered |
| | IB G3 | Pelvic radiotherapy |
| | | If negative prognostic factors combination of radiation and chemotherapy could be considered |
| Stage II | | Pelvic radiotherapy and- vaginal brachytherapy |
| | | If grade 1–2 tumor, myometrial invasion <50%, negative LVSI and complete surgical staging: brachytherapy alone |
| | | If negative prognostic factors: chemotherapy ± radiation |
| Stage III–IV | | Chemotherapy |
| | | If positive nodes: sequential radiotherapy |
| | | If metastatic disease: chemotherapy–radiotherapy for palliative treatment |

# Uusiutunut EC IGCS ja ESCO 2009

TABLE 1. Proposal for management of recurrent endometrioid endometrial carcinoma

| Site of Recurrent Disease | Recommendation | Alternative Approaches | |
|---|---|---|---|
| Local | | | |
| In irradiated area | Surgical cytoreduction (compromising pelvic exenteration) followed by radiotherapy on individual basis | Surgical cytoreduction and in case of microscopically positive margins, combined with intraoperative radiotherapy | Palliative reirradiation |
| In radiotherapy-naive area | Pelvic radiotherapy and/or brachytherapy | Surgical cytoreduction (compromising pelvic exenteration) followed by radiotherapy and/or systemic therapy on individual basis | In cases of large primarily unresectable tumors: neoadjuvant or induction chemotherapy followed by surgery and/or radiotherapy |
| Regional | | | |
| Pelvic recurrence | | | |
| In irradiated area | Surgical cytoreduction if disease is completely resectable | Surgical cytoreduction with IORT or combined operative and radiotherapeutic treatment if no disease or only microscopic disease remains | |
| In radiotherapy-naive area | Pelvic radiotherapy with or without prior complete surgical cytoreduction | Extensive surgical cytoreduction if disease seems completely resectable | Neoadjuvant or induction chemotherapy followed by surgery or radiotherapy |
| Abdominal or peritoneal recurrence | Systemic therapy with or without debulking surgery and/or radiotherapy | Surgical cytoreduction with or without HIPEC | |
| Distant | Systemic therapy (chemotherapy or hormone therapy) | Systemic therapy (chemotherapy or hormone therapy) with or without metastasectomy or local radiotherapy | Palliative radiotherapy or surgery |

# Seuranta

- Peruste seurannalle
  - uusiutumisen toteaminen
  - hoidon haittavaikutuksien minimointi
    - sekundaarisyövän ehkäisy
    - psyykinen, fyysinen ja sosiaalinen tuki
- Huomioi altistavat tekijät
  - DM, obesiteetti, kardivaskulaarisairaudet liikunta

# Seuranta käynnillä

- Keskustelu
  - Psyykinen tuki
    - Positiivinen asenne, toivo
- Gyn tutkimus, abd palpaatio, imusolmukkeet
- Kuvantaminen ja markkerit kliinisen harkinnan mukaan

# Sairastetun EC jälkeinen HRT

- Premenopausaaliset
  - Matalan riskin EC ei estettä
    - Huom Ei:  gr3 endometriumin strooma sarkooma
- Postmenopausaaliset
  - Indikaatiot kuten edellä huomioiden yleiset kriteerit HRT:sta