Endometrial Cancer Screening Options and Diagnostics

Date: 29.09.2023; 12:50 – 13:30
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UNIWERSYTECKIE CENTRUM ONKOLOGII
Uniwersytecki Szpital Kliniczny w Białymstoku

ESGO Certified Centre in Ovarian Cancer Surgery

ESGO Centre of Excellence in Endometrial Cancer Surgery
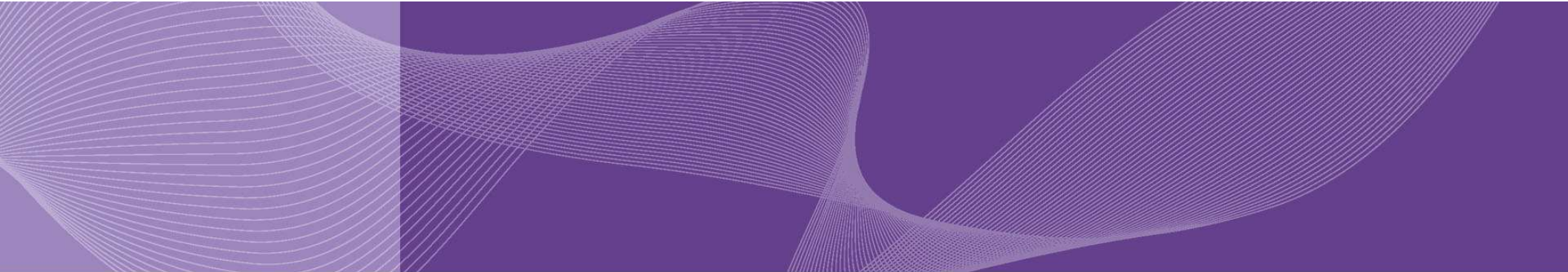
No conflict of interest
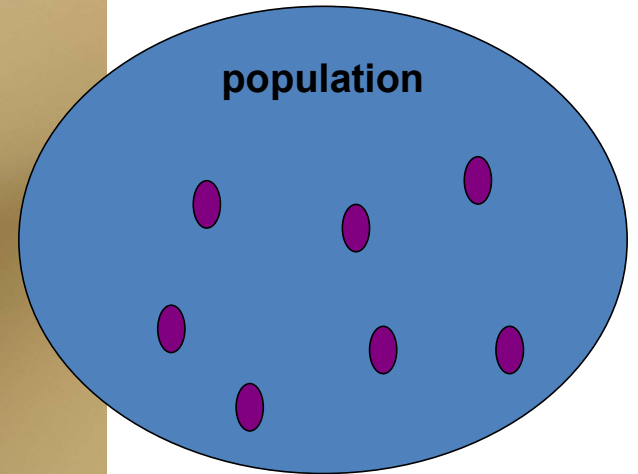
Everyones very good know, that…

EASY

SIMPLE

- Rocognized in early stages - (FIGO Ia, Ib)
- … bacause of very early symptoms
- … and whole gynae. and gynae. oncol. now how to do it!!!

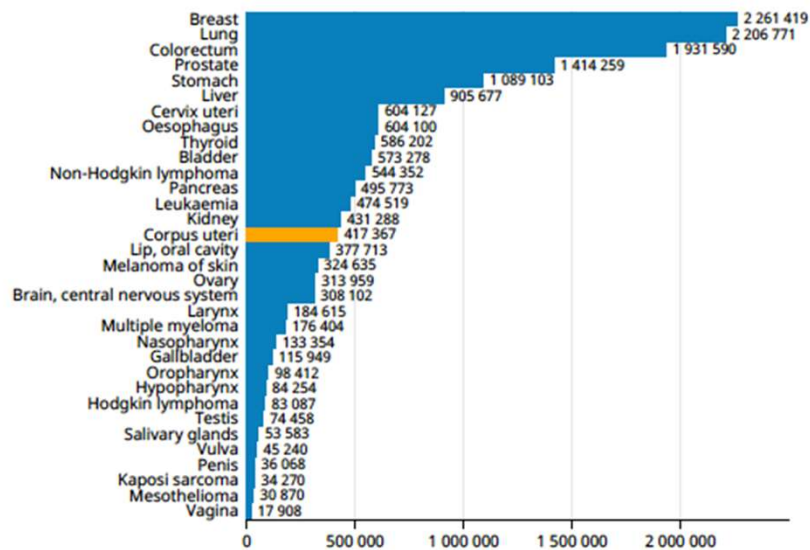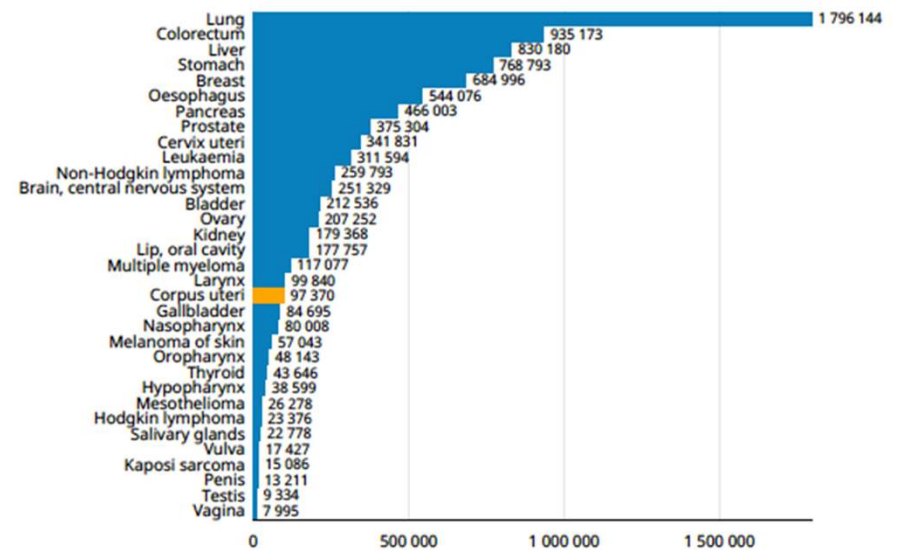# Corpus uteri
Source: Globocan 2020

## Number of new cases in 2020, both sexes, all ages

Site	Cases
Breast	2 261 419
Lung	2 206 771
Colorectum	1 931 590
Prostate	1 414 259
Stomach	1 089 103
Liver	905 677
Cervix uteri	604 127
Oesophagus	604 100
Thyroid	586 202
Bladder	573 278
Non-Hodgkin lymphoma	544 352
Pancreas	495 773
Leukaemia	474 519
Kidney	431 288
Corpus uteri	417 367
Lip, oral cavity	377 713
Melanoma of skin	324 635
Ovary	313 959
Brain, central nervous system	308 102
Larynx	184 615
Multiple myeloma	176 404
Nasopharynx	133 354
Gallbladder	115 949
Oropharynx	98 412
Hypopharynx	84 254
Hodgkin lymphoma	83 087
Testis	74 458
Salivary glands	53 583
Vulva	45 240
Penis	36 068
Kaposi sarcoma	34 270
Mesothelioma	30 870
Vagina	17 908

Number of deaths in 2020, both sexes, all ages

Site	Deaths
Lung	1 796 144
Colorectum	935 173
Liver	830 180
Stomach	768 793
Breast	684 996
Oesophagus	544 076
Pancreas	466 003
Prostate	375 304
Cervix uteri	341 831
Leukaemia	311 594
Non-Hodgkin lymphoma	259 793
Brain, central nervous system	251 329
Bladder	212 536
Ovary	207 252
Kidney	179 368
Lip, oral cavity	177 757
Multiple myeloma	117 077
Larynx	99 840
Corpus uteri	97 370
Gallbladder	84 695
Nasopharynx	80 008
Melanoma of skin	57 043
Oropharynx	48 143
Thyroid	43 646
Hypopharynx	38 599
Mesothelioma	26 278
Hodgkin lymphoma	23 376
Salivary glands	22 778
Vulva	17 427
Kaposi sarcoma	15 086
Penis	13 211
Testis	9 334
Vagina	7 995

Cancer incidence and mortality statistics worldwide and by region

| | Incidence | | | | | | Mortality | | | | | |
| | Both sexes | | Males | | Females | | Both sexes | | Males | | Females | |
	New cases	Cum. risk 0-74 (%)	New cases	Cum. risk 0-74 (%)	New cases	Cum. risk 0-74 (%)	Deaths	Cum. risk 0-74 (%)	Deaths	Cum. risk 0-74 (%)	Deaths	Cum. risk 0-74 (%)
Eastern Africa	3 550	0.38	-	-	3 550	0.38	1 152	0.13	-	-	1 152	0.13
Middle Africa	1 001	0.27	-	-	1 001	0.27	329	0.09	-	-	329	0.09
Northern Africa	3 706	0.43	-	-	3 706	0.43	790	0.09	-	-	790	0.09
Southern Africa	2 342	0.97	-	-	2 342	0.97	645	0.25	-	-	645	0.25
Western Africa	3 425	0.44	-	-	3 425	0.44	1 126	0.15	-	-	1 126	0.15
Caribbean	3 874	1.54	-	-	3 874	1.54	1 184	0.43	-	-	1 184	0.43
Central America	6 675	0.80	-	-	6 675	0.80	1 461	0.19	-	-	1 461	0.19
South America	22 721	0.98	-	-	22 721	0.98	6 073	0.24	-	-	6 073	0.24
Northern America	68 402	2.57	-	-	68 402	2.57	12 789	0.37	-	-	12 789	0.37
Eastern Asia	105 413	0.91	-	-	105 413	0.91	20 745	0.17	-	-	20 745	0.17
South-Eastern Asia	25 423	0.76	-	-	25 423	0.76	7 613	0.23	-	-	7 613	0.23
South-Central Asia	25 573	0.33	-	-	25 573	0.33	9 478	0.12	-	-	9 478	0.12
Western Asia	10 901	1.08	-	-	10 901	1.08	3 159	0.30	-	-	3 159	0.30
Central and Eastern Europe	59 289	2.48	-	-	59 289	2.48	13 613	0.47	-	-	13 613	0.47
Western Europe	28 901	1.61	-	-	28 901	1.61	6 552	0.23	-	-	6 552	0.23
Southern Europe	23 995	1.74	-	-	23 995	1.74	5 643	0.28	-	-	5 643	0.28
Northern Europe	17 866	2.03	-	-	17 866	2.03	4 155	0.32	-	-	4 155	0.32
Australia and New Zealand	3 779	1.79	-	-	3 779	1.79	738	0.25	-	-	738	0.25
Melanesia	436	1.23	-	-	436	1.23	101	0.32	-	-	101	0.32
Polynesia	56	1.87	-	-	56	1.87	16	0.49	-	-	16	0.49
Micronesia	39	1.73	-	-	39	1.73	8	0.28	-	-	8	0.28
Low HDI	7 709	0.37	-	-	7 709	0.37	2 515	0.13	-	-	2 515	0.13
Medium HDI	32 158	0.36	-	-	32 158	0.36	10 904	0.12	-	-	10 904	0.12
High HDI	149 724	0.88	-	-	149 724	0.88	34 694	0.20	-	-	34 694	0.20
Very high HDI	227 503	1.94	-	-	227 503	1.94	49 189	0.31	-	-	49 189	0.31
World	417 367	1.05	-	-	417 367	1.05	97 370	0.22	-	-	97 370	0.22

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Age standardized (World) incidence rates, corpus uteri, all ages

≥ 14.9
10.3–14.9
7.6–10.3
4.1–7.6
2.5–4.1
< 2.5

Not applicable
No data
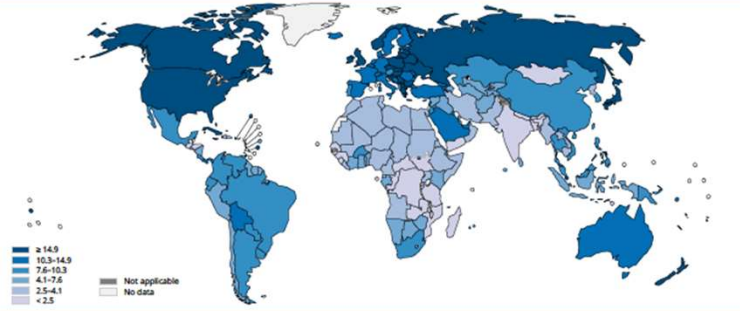
Age standardized (World) mortality rates, corpus uteri, all ages

≥ 3.0
2.2–3.0
1.8–2.2
1.2–1.8
0.82–1.2
< 0.82

Not applicable
No data
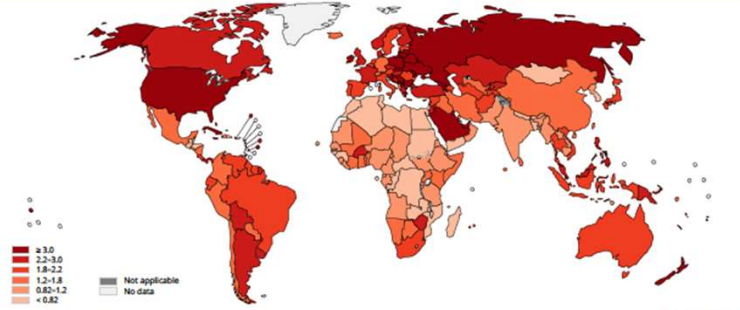
Data source: GLOBOCAN 2020
Graph production: IARC (https://gco.iarc.fr/today)
World Health Organization

World Health Organization
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Cancer Advocacy Groups

Incidence, both sexes
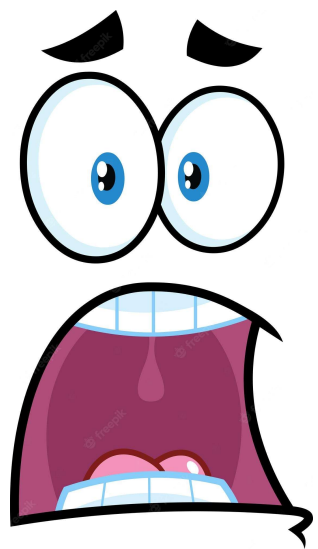
Africa (3.4%)
LAC** (8%)
N.America* (16.4%)
Europe (31.2%)
Asia (40.1%)
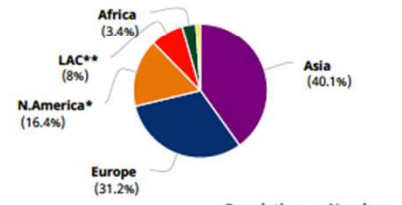
	Population	Number
	Asia	167 310
	Europe	130 051
	*Northern America	68 402
	**Latin America and the Caribbean	33 270
	Africa	14 024
	Oceania	4 310
	Total	417 367

Mortality, both sexes

Africa (4.2%)
LAC** (9%)
N.America* (13.1%)
Europe (30.8%)
Asia (42.1%)
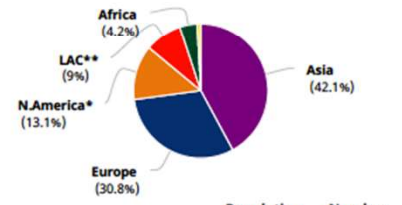
	Population	Number
	Asia	40 995
	Europe	29 963
	*Northern America	12 789
	**Latin America and the Caribbean	8 718
	Africa	4 042
	Oceania	863
	Total	97 370

5-year prevalence, both sexes

Africa (2.5%)
LAC** (7.5%)
N.America* (18.9%)
Europe (34.1%)
Asia (35.9%)
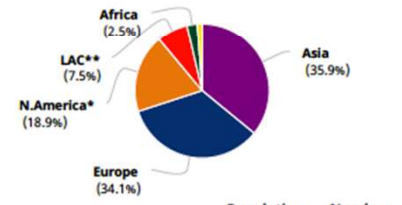
	Population	Number
	Asia	508 022
	Europe	482 952
	*Northern America	267 491
	**Latin America and the Caribbean	105 553
	Africa	34 895
	Oceania	16 300
	Total	1 415 213

Why do we have to worry…, do we??

SLN
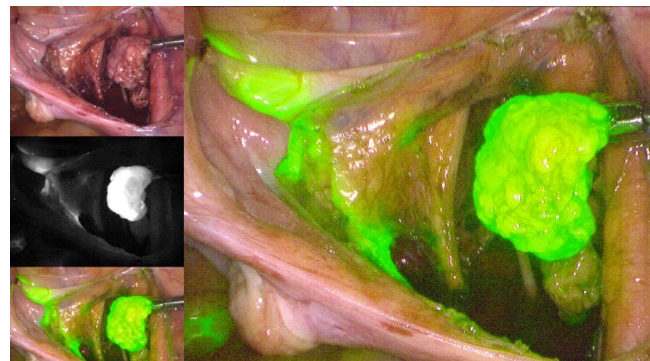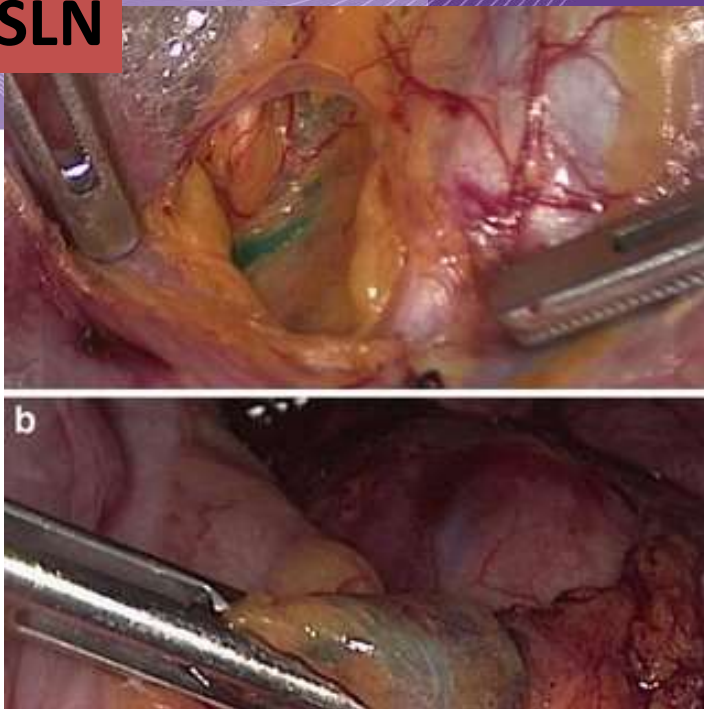
- **21% of cases give mts to regional lymphatic nodes**
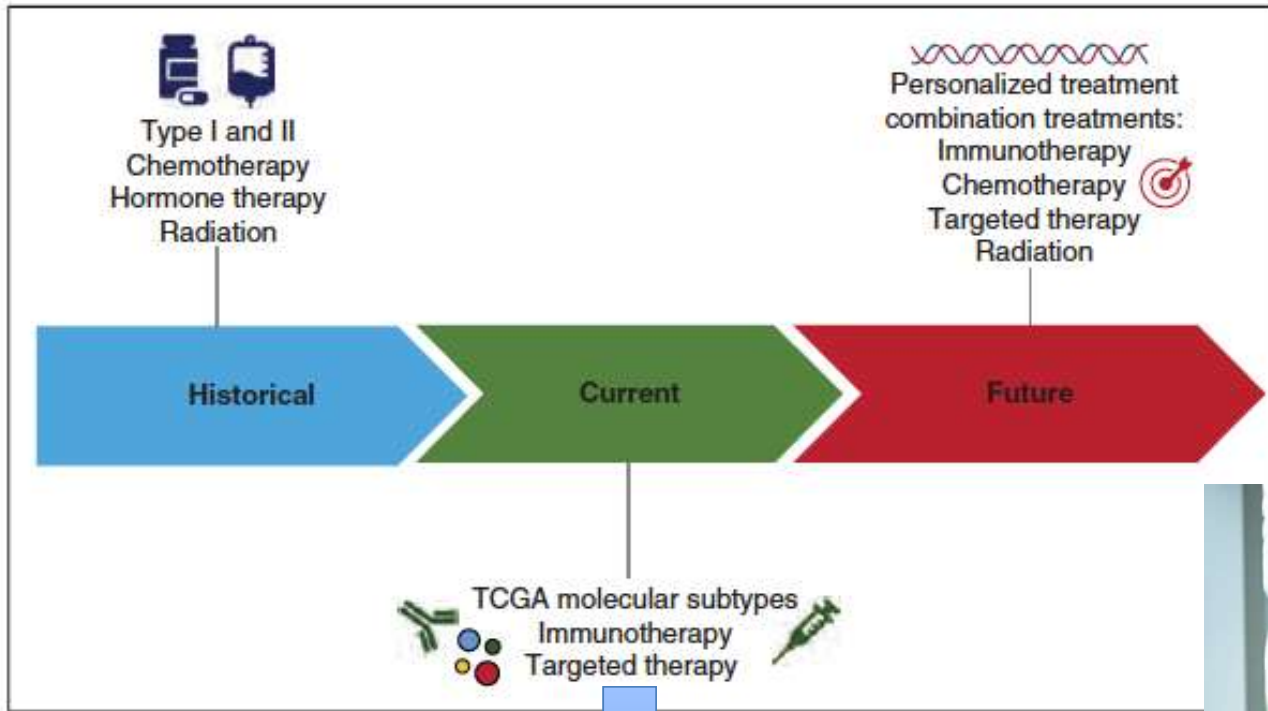
9% of cases – distant mts!!

Historically, endometrial cancer (EC):

- Type I – endometrioid adenocarcinoma (80-90%)
- Type II – non-endometrioid subtypes (serous, clear cell, undifferentiated ca, carcinosarcoma/malignat-mixed Mullerian Tu)

Molecular data ----- integral component of pathologic evaluation:
- Type I associated with genetic alterations in PTEN, KRAS, CTNNB1, PIK3CA MLH1 promoter hypermethylation
- Serous cancer (Type II): mut. TP53

Limitations of that dualistic model: 25% HG endometrioid Ca – express mut. PT53 and behave like serous Ca

Kandoth C, Schultz N, Cherniack AD, et al. Integrated genomic characterization of endometrial carcinoma. Nature 2013;497:67–73.

Type I and II
Chemotherapy
Hormone therapy
Radiation

Personalized treatment
combination treatments:
Immunotherapy
Chemotherapy
Targeted therapy
Radiation

Historical | Current | Future

TCGA molecular subtypes
Immunotherapy
Targeted therapy

Kashermann i wsp. Future Oncol. 10.2217/fon-2020-0655

- POLE – ultramutated Tu
- Microsatellite unstable Tu
- Copy-number high tumours with mostly TP53 mut.
- Remaining group without these alteration

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Reid-Nicholson M, Iyengar P, Hummer AJ, et al. Immunophenotypic diversity of endometrial adenocarcinomas: implications for differential diagnosis. Mod Pathol 2006;19:1091–100.

Risk factors

- High BMI (Obesity): RR (relative risk) of EC – 1.89 (95%CI: 1.34 – 2.67, p<0.0001);
- Metabolic syndrome (RR – 2.21, p<0.001):
    1. Overweight
    2. Obesity
    3. Hypertension
    4. Hypertriglyceridemia;
- Diabetes mellitus – **is not** an independent risk factor (link with obesity);
- Nulliparity, early menarche, late menopause
- Infertility (PCOS: 3-fold increasing in risk);
- Unopposed oestrogen therapy (10- to 30-fold, if treatment cont. 5 or more years);
- Oestrogen-producing tumours, Ovarian granulosa Tu, Theca cell Tu;
- Tamoxifen treatment (RR depent on pre- postmenopausal women)
- Genetic: Lynch Syndrome, HNPCC (Hereditary Non-Polyposis Colorectal Cancer) – mut. in DNA mismatch repair genes **(MLH1, MSH2, MSH6, PMS2)**

The classic symptom of EC – **abnormal uterine bleeding**

Prticular suspicion should be held for:

- Postmenopausal women;
- Women aged 40 years and over with high-risk factors;
- With vaginal discharge;
- Have a thickened endometrium incidentally noted on US scan;
- Abnormal cervical cytology smear (AGUS, AIS)
- Patient with intraperitoneal disease:
  - ✓ Abdominal distention
  - ✓ Pelvic preassure
  - ✓ Lower abdominal or abdominal pain.

Zhang Y, Liu H, Yang S, et al. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers 2014;29:e21–9.

Symptomatic women

Asymptomatic women

Asymptomatic women

ESMO-ESGO-ESTRO protocol:

- Women with average risk for endometrial cancer
- Women at increased risk for endometrial cancer
- Women with high risk for endometrial cancer

Asymptomatic women - with average risk for endometrial cancer

- No indication that population-based screening has a role in early detection of EC
- No standard or routine test for EC
- No evidence for screening by ultrasonography (EV, TV) in reducing mortality rate
  - ◇ Unnecessary additional biopsies bacause of false-positive test results
- Menopausal women – should be strongly encourage to report any abnormal bleeding

Smith RA, Cokkinides V, Brawley OW. Cancer screening in the United States, 2009: a review of current American Cancer Society guidelines and issues in cancer screening. CA Cancer J Clin 2009;59:27–41.

Asymptomatic women – increased risk for endometrial cancer

- Patients with risk factors should be informed of the risk and symptoms of EC
- Patients with risk of EC and:
  - o Endometrial thickening
  - o Positive findings in US (increased vascularity, inhomogeneity of the endometrium particulate fluid, thickened endometrium over 11mm
- should be managed on a case-by-case basis
- Premenopausal women treated by Tamoxifen need routine gyn. care
  - o Shoud be informed about risk of AEH or EC

Asymptomatic women – high risk for endometrial cancer

- Known carriers of HNPCC-associated genetic mutation; Lynch Syndrome
- Substantial likelihood of being a mutation carrier
- Women without genetic testing results – families suspected of dominant predisposition to colon cancer

Medical Interview

Manchanda R, Saridogan E, Abdelraheim A, et al. Annual outpatient hysteroscopy and endometrial sampling (OHES) in HNPCC/Lynch syndrome (LS). Arch Gynecol Obstet 2012;286:1555–62.

Mandatory pre-operative work-up
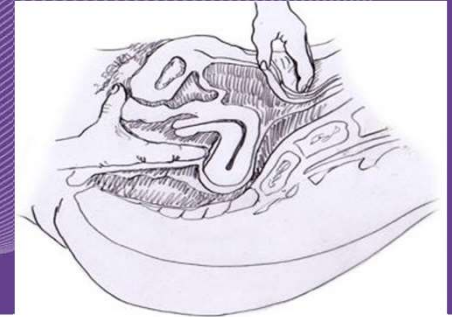
Pelvic examination and pelvic US scan – to evaluate clincal staging of EC (FIGO) before definitive pathology

Transvaginal
Transrectal

First imaging procedure to evaluate abnornal bleeding:
- done by expert sonographer
- evaluating the size of the tumour
- ruling out ovarian disease
- assessing myometrial invasion and cervical stroma invasion

Eriksson LS, Lindqvist PG, Flöter Rådestad A, et al. Transvaginal ultrasound assessment of myometrial and cervical stromal invasion in women with endometrial cancer: interobserver reproducibility among ultrasound experts and gynecologists. Ultrasound Obstet Gynecol 2015;45:476–82.

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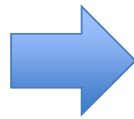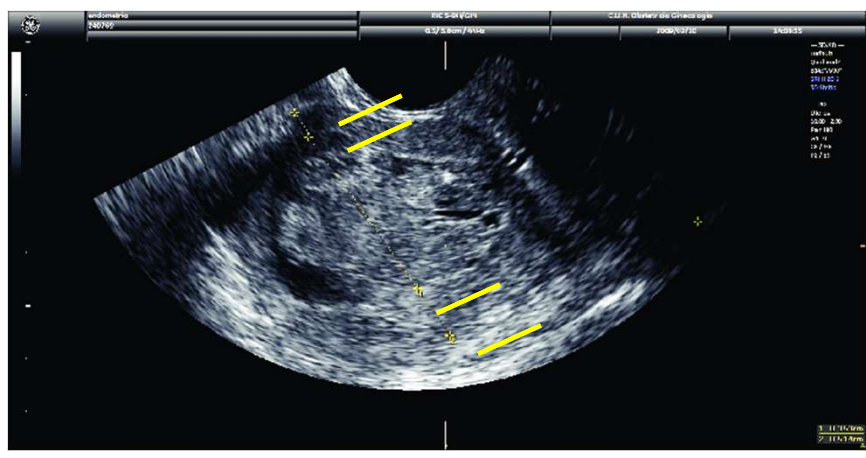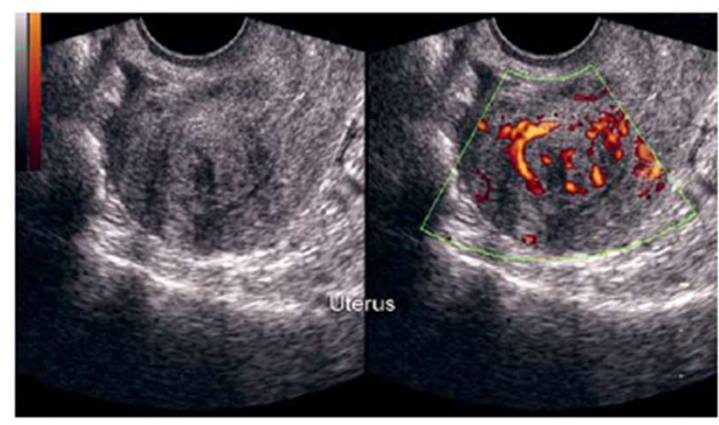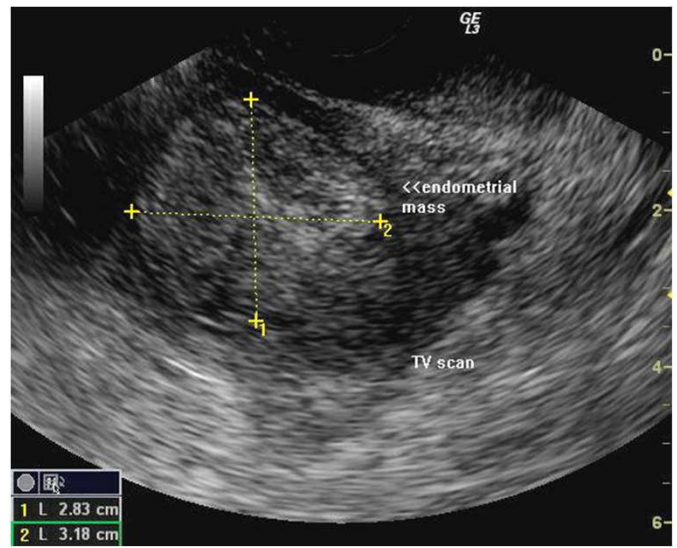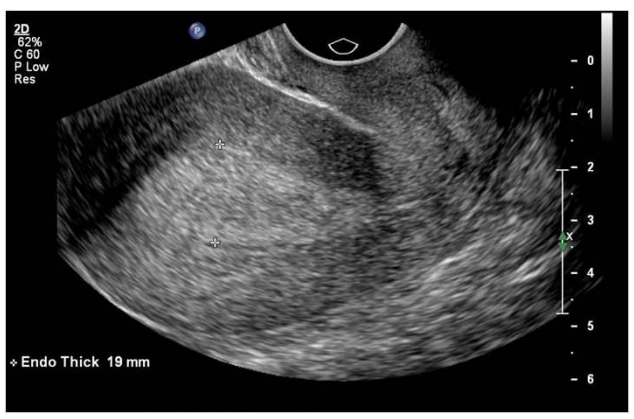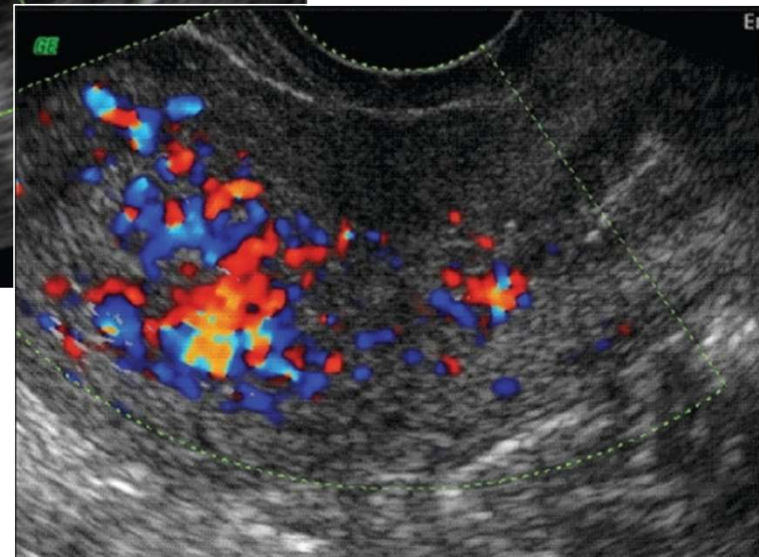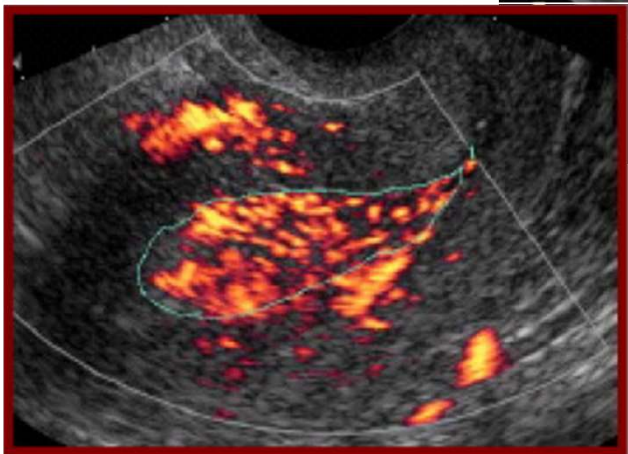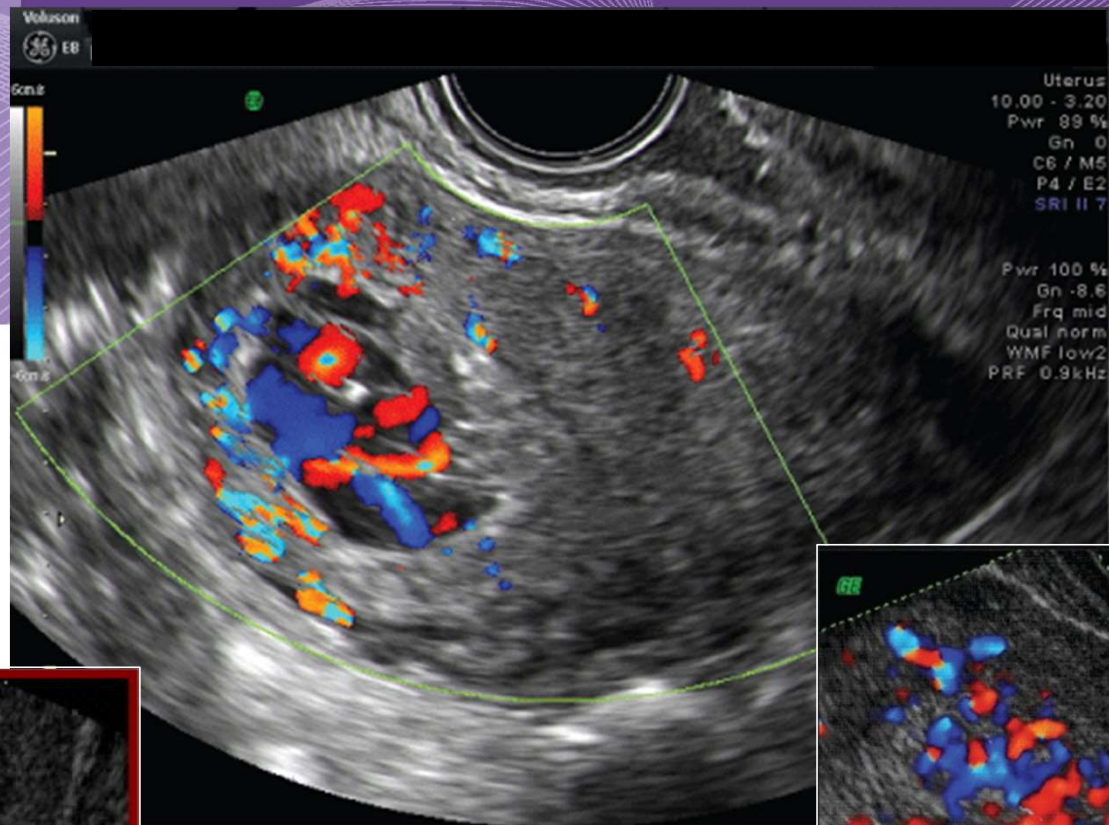
3D diagnostic of EC
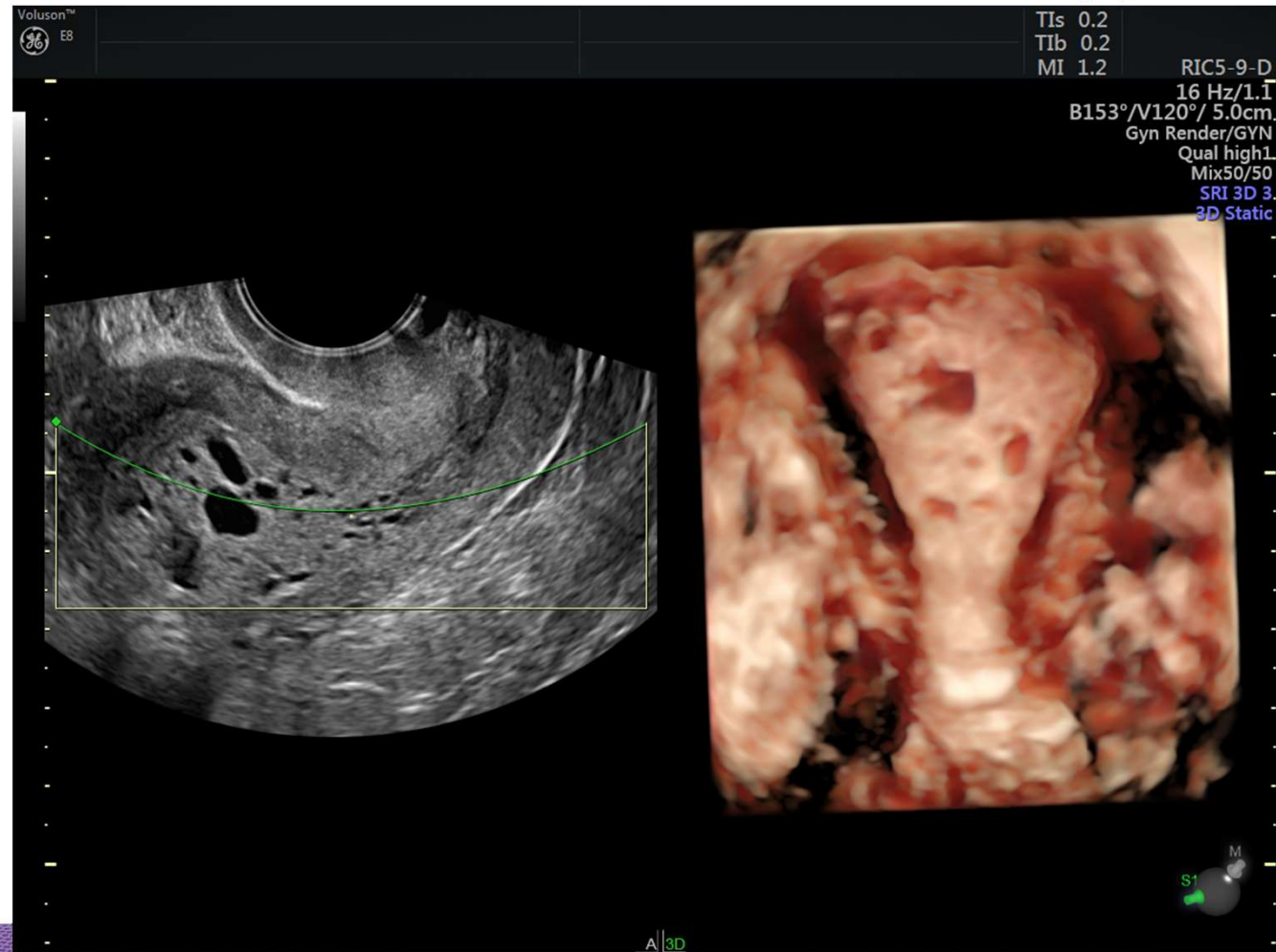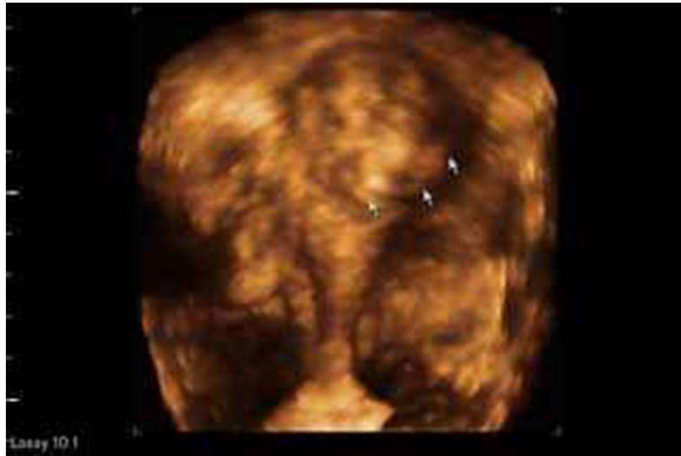
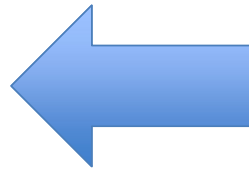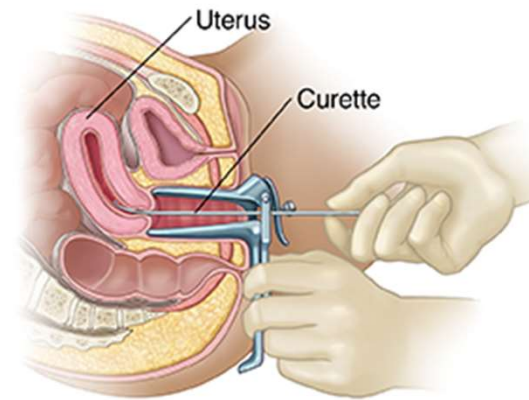## Pre-operative pathological information is crucial for establishing the surgical plan.

The final therapeutic strategy could be based on the information available before surgery:

- Stage (apparent I or more advanced stage)
- Grade (G1, G2, G3)
- Histotype (endometroid or non-endometrioid tumour)

Pathologic evaluation of the endometrium

- Endometrial cancer
- Other etiologies:
  - Chronic endometritis
  - Atrophy
  - Polyps
  - Cervical cancer
  - Unusual histologic variants:
    - Carcinosarcoma
    - Serous carcinoma
    - Placental nodule

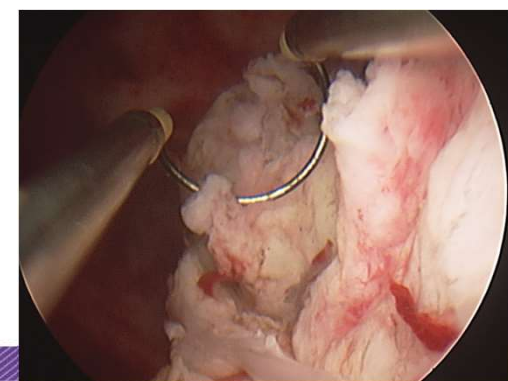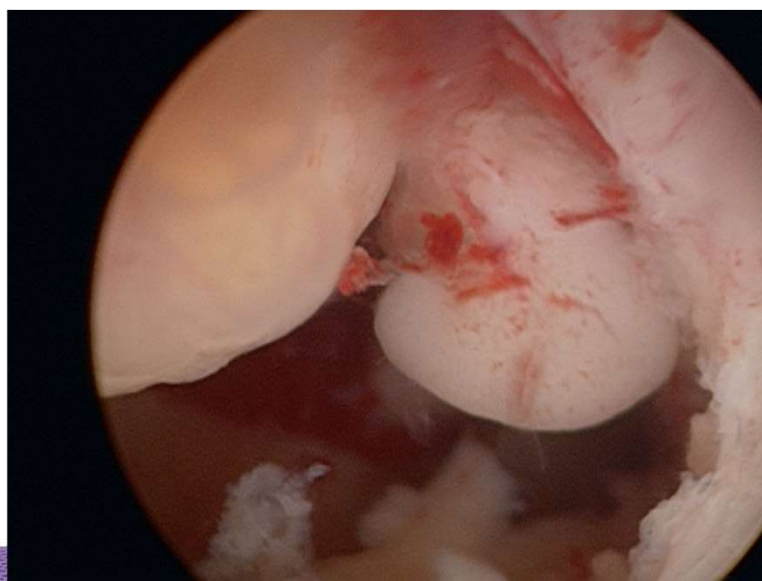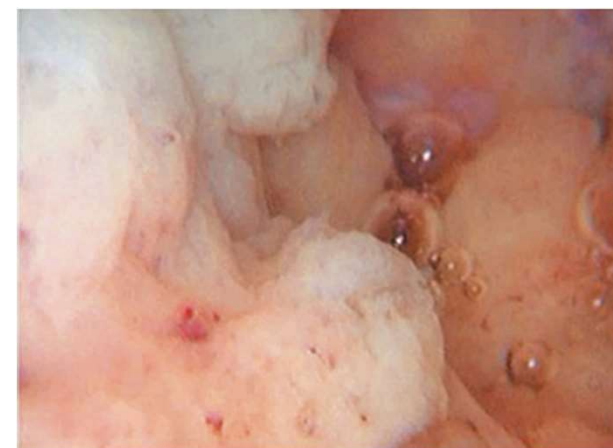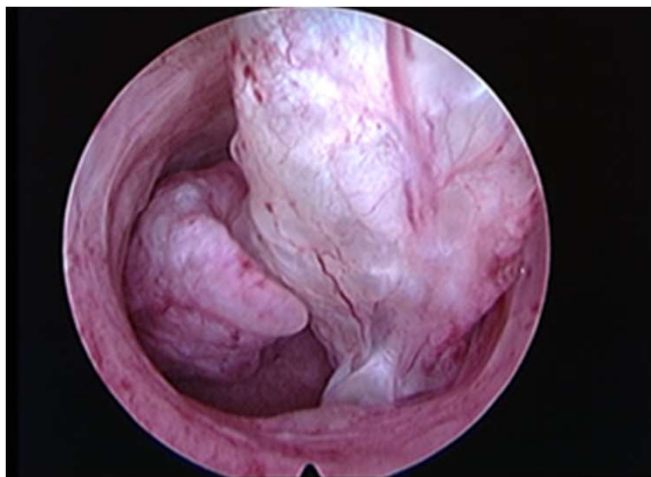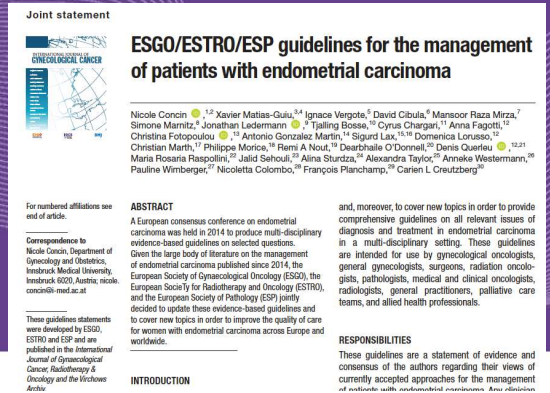D&C – Dilatation and Curattege
EMB - Office Endometrial Biopsy

Tissue evaluation

EMB and D&C offer similar histological information when adequate performed

Hysteroscopy

Optional pre-operative work-up

ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma

Additional imaging diagnostic ⟶ clinical situation

Apperent stage I of EC ---------------- MRI to evaluate myometrial invasion

only in the institutions where the indication for LND is tailored according to the stratification of patients into low-, intermediate- and high-risk groups

Advanced EC --------------------------- MTI, CT, PET-CT

Expert sonographer

consider to assess ovarian, nodal, peritoneal or metastatic disease

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Serum tumour markers

Ca-125 and HE4 (Human epididymis protein 4)

significantly corelate

- Histological grade
- Stage
- Lympho node metastasis
- Myometrial invasion
- Cervical involvement

There is no evidence for clinical usefulness of serum tumour markers

Antonsen SL, Høgdall E, Christensen IJ, et al. HE4 and CA125 levels in the preoperative assessment of endometrial cancer patients: a prospective multicenter study (ENDOMET). Acta Obstet Gynecol Scand 2013;92:1313–22.

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