Gynecological cancer - Lynch syndrome (LS) testing strategies

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Background

- Approx. 3% of all patients with Endometrial cancer (EC) have Lynch Syndrome (LS) [1.2]
- 50% of women with LS get EC and/or ovarian cancer (OC) as the first cancer and it takes 10-15 years before they develop their Colorectal cancer (CRC)[3]
- Early identification through genetic testing in all woman with EC/OC is very important to ensure these patients and their relatives attendance in the screening programs.

[1] *Hampel H, Frankel WL, Martin E, Arnold M, Khanduja K, Kuebler P, et al. Screening for the Lynch syndrome (hereditary nonpolyposis colorectal cancer). The New England journal of medicine. 2005;352(18):1851-60.*

[2] *28. Ryan NAJ, McMahon R, Tobi S, Snowsill T, Esquibel S, Wallace AJ, et al. The proportion of endometrial tumours associated with Lynch syndrome (PETALS): A prospective cross-sectional study. PLoS Med. 2020;17(9):e1003263.*

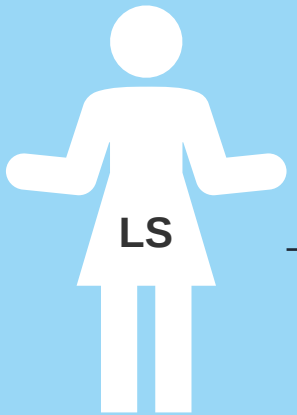
[3] *Lu KH, Dinh M, Kohlmann W, Watson P, Green J, Syngal S, et al. Gynecologic cancer as a "sentinel cancer" for women with hereditary nonpolyposis colorectal cancer syndrome. Obstet Gynecol. 2005;105(3):569-74.*

Cumulative lifetime risk at the age of 75 for LS risk persons[1]

Pathogenic variant of	***MLH1***	***MSH2***	***MSH6***	***PMS2***
KRC	48% (K) 57% (M)	47% (K) 51% (M)	20% (K) 18% (M)	10% (Both genders)
EC	37%	49%	41%	13%
OC	11%	17%	11%	3%

[1]*Cancer risks by gene, age, and gender in 6350 carriers of pathogenic mismatch repair variants: findings from the prospective Lynch syndrome Database. Genetics in medicine: official journal of the American College of Medical Genetics. 2020;22(1):15-25*

Gynecological screening



Screening – 1.visit

- GU
- Patient education: alarm symptoms
- Risk of Cancer (MMR / Family history)
- Gyn. screening starts when colonoscopy start

≥ 35 years
Every 2nd year
GU
TVUL (thickness of the endometrium, flow and other signs of pathology, ovarian pathology, ascites)

Alarm symptoms

Bleeding disorders:

- Menorrhagia
- Metorrhagia
- Post menopausal hemorrhage

Other symptoms:

- Abdominal symptoms: pain, bloated stomach, changes in bowel habits
- Bladder symptoms

Invasive examination of the endometrium (vabra)

- only if pathological findings or alarm symptoms are present

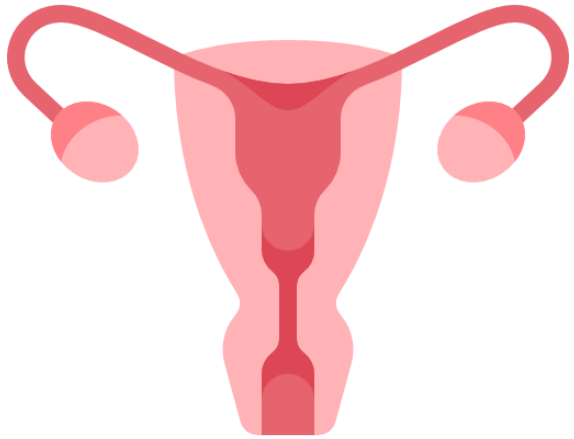
CA-125

- only if pathological findings or alarm symptoms are present

Hysterectomy and bilateral salpingo-oophorectomy(BSO)

Prophylactic hysterectomy and BSO may be offered depending on pathogenic MMR variant, age and fertility history

- In case of bowel resection due to CRC
- After the end of the fertility wish or after the age of 40
- Followed by hormone replacement counseling



Take home message

- 50% of women with LS get EC and/or OC as the first cancer and it takes 10-15 years before they develop CRC – gynaecological cancer at a young age
- Screening: ≥ 35 years - Every 2nd year- GU / TVUL, tests according to symptoms and findings.
- Patient education: Alarm Symptoms!
- Prophylactic hysterectomy and BSO is a possibility

Thank you for your time

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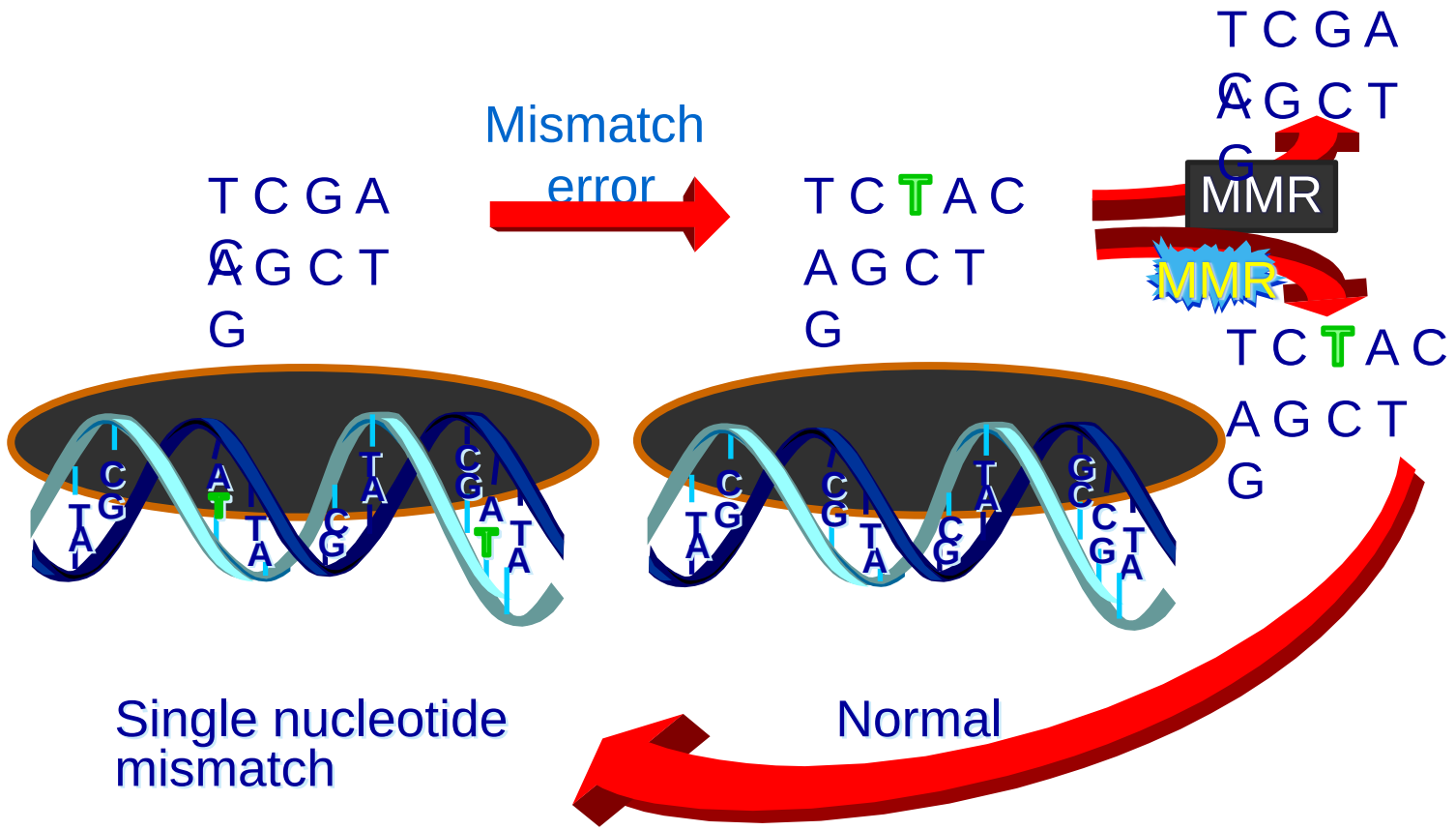
DNA Mismatch repair (MMR)



Who needs the gynaecological screening?

Clinical screening

- Gynecological screening is only recommended for women with LS (B)
- LS-risk persons who have not had gynecological cancer should be referred for a gynecological examination and an informational interview about warning symptoms, gynecological cancer risk and screening programs when starting colonoscopy screening (D)
- LS-risk persons must be informed of their MMR-specific cancer risk, interpreted in relation to the family history (D)

Background

Lynch syndrom

- **Hyppigste arvelig tarm og gynækologisk cancersyndrom**
- **Patienter får deres cancer i en tidlige alder**
- **Halvdelen af kvinder får deres EC/OC 10-15 år inden de får KRC**
- **Vigtigt at identificere disse højrisiko patienter, så de og deres familie kan opstarte koloskopiscreening og dermed reducere deres mortalitet fra tarmkræft**

Anbefalinger

Clinical screening programs

- LS risk persons ≥ 35 years of age are recommended gynecological screenings (GU and TVUL) every 2 years.
- In case of abnormal bleeding (meno- and metrorrhagia, postmenopausal bleeding) and/or pathological findings on ultrasound, an endometrial biopsy is recommended (D))
- Routine endometrial biopsy is not recommended, as there is no evidence that invasive examination of the endometrium is better as a screening method than attention to symptoms and rapid investigation in the event of alarm symptoms (D)
- Measurement of CA-125 is only recommended in case of pathological findings at US (D)

Anbefalinger

Baggrund og udredning

- Detaljeret familieanamnese samt MMR-status bør foreligge på alle patienter med adenokarcinomer i kolon/rektum, tyndtarm, **endometrie, ovarie,** samt invasive og ikke-invasive uroteliale tumorer i øvre urinveje og sebaceøse hudtumorer mhp. identifikation af højrisikogrupper (B)
- Patienter med MMR defekt i tumor, ophobning af cancer i familien eller KRC < 50 år bør henvises til genetisk udredning (B)
- LS-risikopersoner skal informeres om deres MMR-specifikke cancerrisiko, tolket i forhold til familieanamnesen (D)

Anbefalinger

Profylakse

- Profylaktisk behandling med 75-100 mg acetylsalicylsyre kan overvejes til LS-risikopersoner (D)
- Information om væsentlige livstilsfaktorer kan drøftes med risikopersoner, som er arveligt disponeret for KRC (D)

Anbefalinger

Indberetning

Alle resultater af genetisk udredning, behandling og screening bør indberettes til HNPCC-registret (D)

Tak for opmærksomheden