

Re-introducing urothelial cancer screening for Lynch syndrome individuals (new guidelines)

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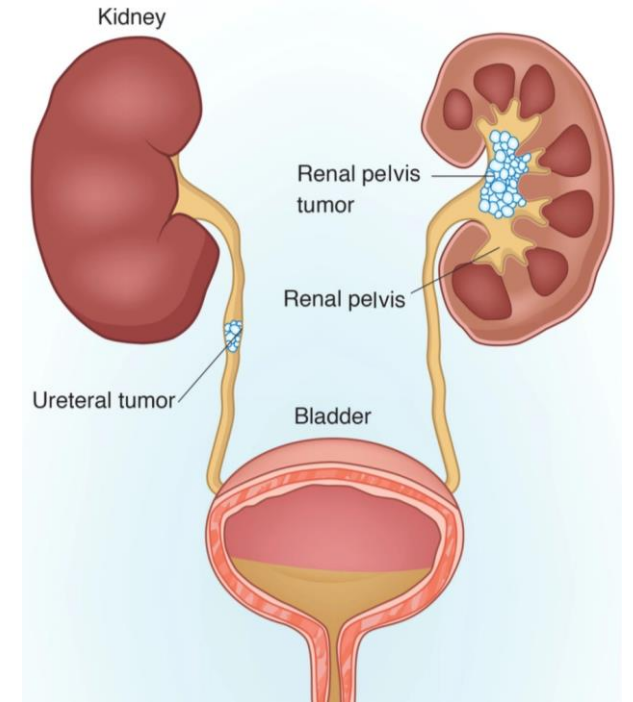
Urothelial cancer in Lynch Syndrome

Upper tract urothelial cancer (UTUC)

- The third-most prevalent cancer in LS



~ 150 UTUC/year
4-8 % are diagnosed in
LS patients registered in
the HNPCC-register

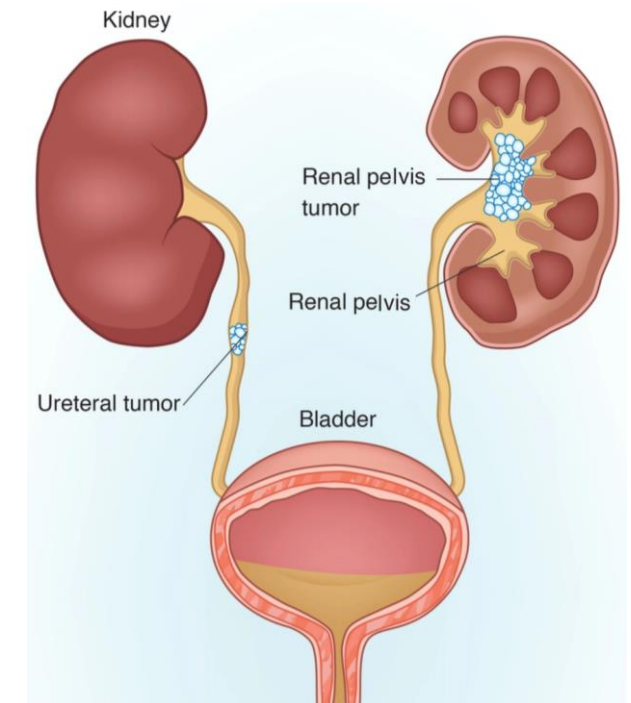


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- Life-time individual risk of 2.9% - 28%

Lynch syndrome (LS)*				
Pathogenic variant in	<i>MLH1</i>	<i>MSH2</i>	<i>MSH6</i>	<i>PMS2</i>
Cancer risk	4% (women) 5% (men)	19% (women) 18% (men)	6% (women) 2% (men)	4% (both sexes)



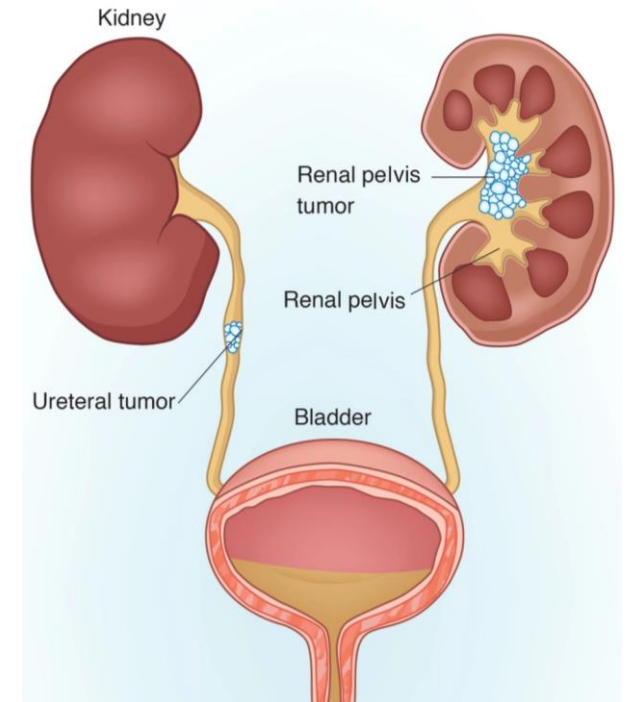
*Dominguez-Valentin M, Sampson JR, Seppala TT, Ten Broeke SW, Plazzer JP, Nakken S, et al. Cancer risks by gene, age, and gender in 6350 carriers of pathogenic mismatch repair variants: findings from the Prospective Lynch Syndrome Database. *Genetics in medicine : official journal of the American College of Medical Genetics*. 2020;22(1):15-25.

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Sporadic UTUC: ~ 65% men
LS-ass. UTUC : ~ 50% men*

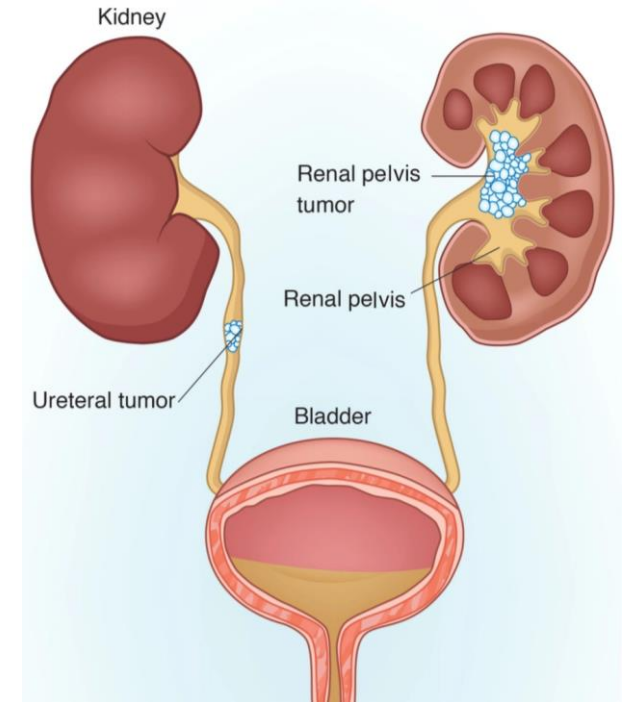


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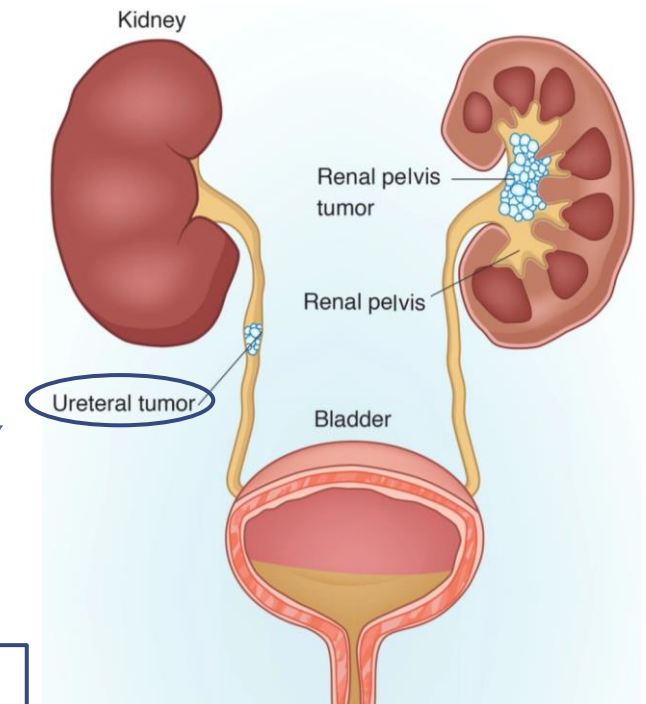
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- Higher proportion of ureteral localization*

51% vs. 28% in sporadic UTUC

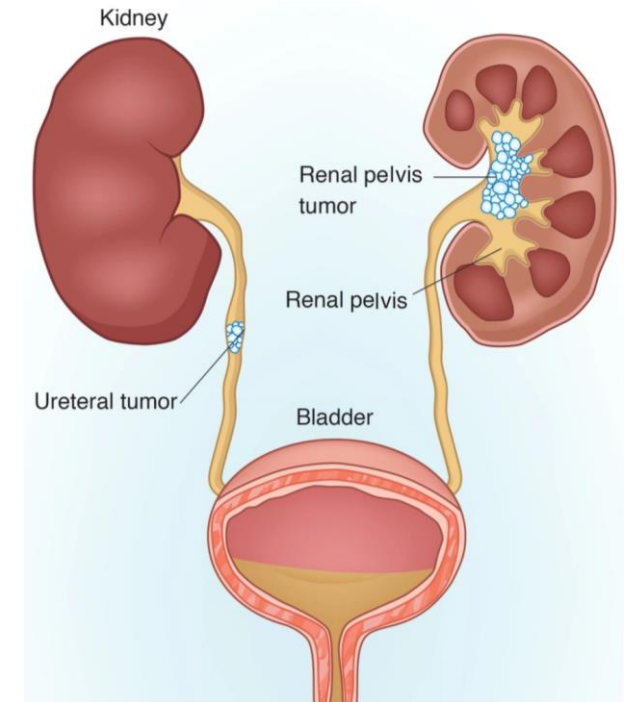


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- Life-time individual risk of 2.9% - 28%
- Women are more likely to be affected than in sporadic UTUC*
- Diagnosed at a younger age (62 vs. 70 years)*
- Higher proportion of ureteral localization*
- Higher risk of bilateral tumors*



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Urothelial cancer in Lynch Syndrome

Bladder cancer

- Contradicting results in regard to the risk of bladder cancer in LS
- Intraluminal seeding from the initial UTUC tumor?
- No recommendation on screening for bladder cancer in LS
- LS with a history of UTUC are followed with cystoscopy, urine cytology and CT urography (similar to non-LS patients)



Urological cancers in Lynch Syndrome

Prostate cancer

- Several studies have shown an association between LS and prostate cancer
- The presumed LS-associated PC does not seem to occur at an earlier age or being more advanced at diagnosis
- No sufficient evidence to support screening for prostate cancer in LS

Testicular cancer

- No clear association

Renal cancer

- One old study has shown an increased renal cell carcinoma risk in a large series of LS patients compared to the general population

International guidelines

No consensus regarding a clear pathway for screening in the literature.

European Association of Urology:

- Highest rates of undiagnosed genetic disease in urological cancers
- Selection of patients with UTUC for Lynch syndrome screening during the first medical interview
- Close monitoring and follow-up
- No recommendations on urothelial cancer screening for LS

National Comprehensive Cancer Network (NCCN):

- Insufficient evidence to recommend a particular surveillance strategy
- Surveillance may be considered in selected individuals such as with a family history of urothelial cancer.
- Individuals with MSH2 pathogenic variants (especially males) appear to be at higher risk
- Surveillance options may include annual urinalysis starting at age 30–35 y

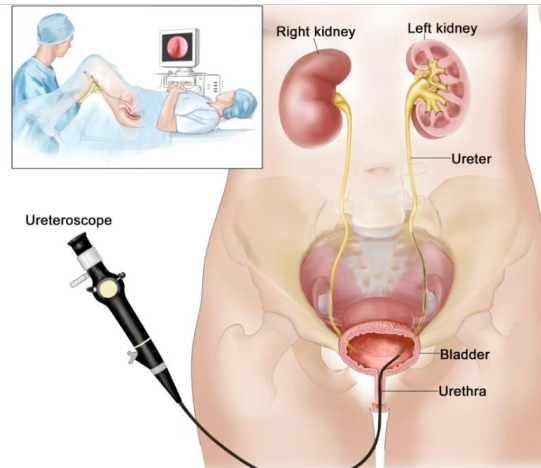
Lynch Syndrome: A Primer for Urologists and Panel Recommendations

Maureen Mork, Scott G. Hubosky, Morgan Rouprêt, Vitaly Margulis, Jay Raman, Yair Lotan, Timothy O'Brien, Nancy You, Shahrokh F. Shariat* and Surena F. Matin†

- A review of the available published literature and guidelines from 1998 to 2014 on Lynch syndrome and its association with upper tract urothelial carcinoma
 - Recommendations based on the literature and the consensus of expert opinion are provided.

The ideal surveillance panel?

- Upper tract visualization necessitates greater invasiveness along with radiation exposure and possibly anesthesia



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The ideal surveillance panel?

- Upper tract visualization necessitates greater invasiveness along with radiation exposure and possibly anesthesia
- Urine cytology
- Urinalyses (microscopic haematuria)
- Contrast CT urography
- Renal Ultrasound

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- Urinalyses
- Urine cytology (not alone)
- CTU (if it is already done for follow-up of colon cancer)

More intensive screening of high risk LS populations, particularly those with MSH2 mutation or family history of UTUC, is recommended.

We encourage urologists to use individual judgment on the risks and rewards of upper tract assessment vs the potential for missing a diagnosis

New guidelines



Arvelig disposition for kolorektalcancer,
Lynch syndrom, FCC og let øget risiko
– Udredning, behandling og screeningsprogrammer



Version 2.0

GODKENDT
Faglig godkendelse
3. juni 2022 (DMCG)
Administrativ godkendelse
7. juni 2022 (Sekretariatet for Kliniske
Retningslinjer på Kræftområdet)

REVISION
Planlagt: 1. juni 2024

INDEKSERING
Kolorektalcancer, arvelig kræft, kræftpatienter,
udredning, behandling, screeningskontrol

Øvre urinveje:

16. Urologisk screening anbefales kun i udvalgte LS- familier (D)

17. Klinisk screeningsprogram (urinanalyse for blod, urincytologi og ultralydsskanning af nyrerne) for invasive og ikke-invasive uroteliale tumorer i øvre urinveje anbefales årligt for:

- Risikopersoner ≥ 35 år fra LS-familier med en patogen MSH2-variant (D)
- Risikopersoner ≥ 35 år fra andre LS-familier med mindst to personer med invasiv eller ikke-invasiv urotelial tumor i øvre urinveje (D)

Former Guidelines:

Screening af urinvejene anbefales derfor ikke generelt i HNPCC familier, men kun i familier med 2 eller flere personer med ureter eller pelvistumor – ca. 10 familier i Danmark.

Programmet omfatter urincytologi, urinanalyse for blod og ULscanning af nyrerne (39) [IIb].

Thank you for your attention

