URINARY TRACT CANCER SYMPTOMS, SCREENING AND TREATMENT IN PATIENTS WITH LYNCH SYNDROME

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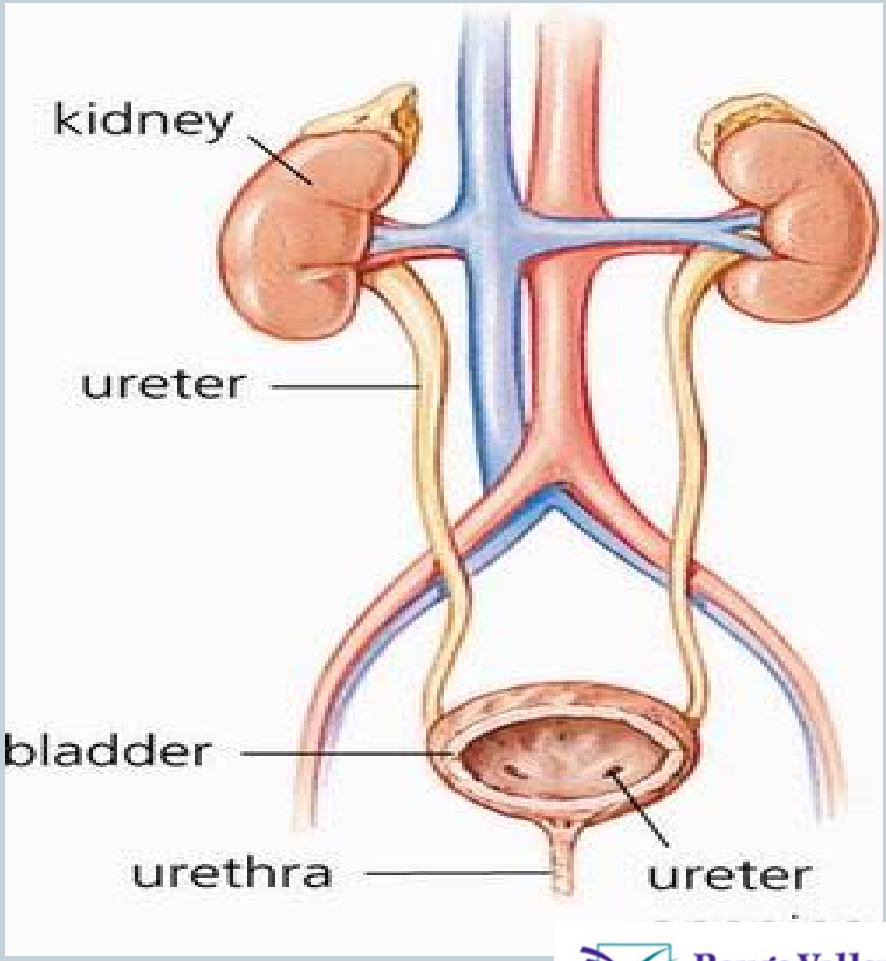
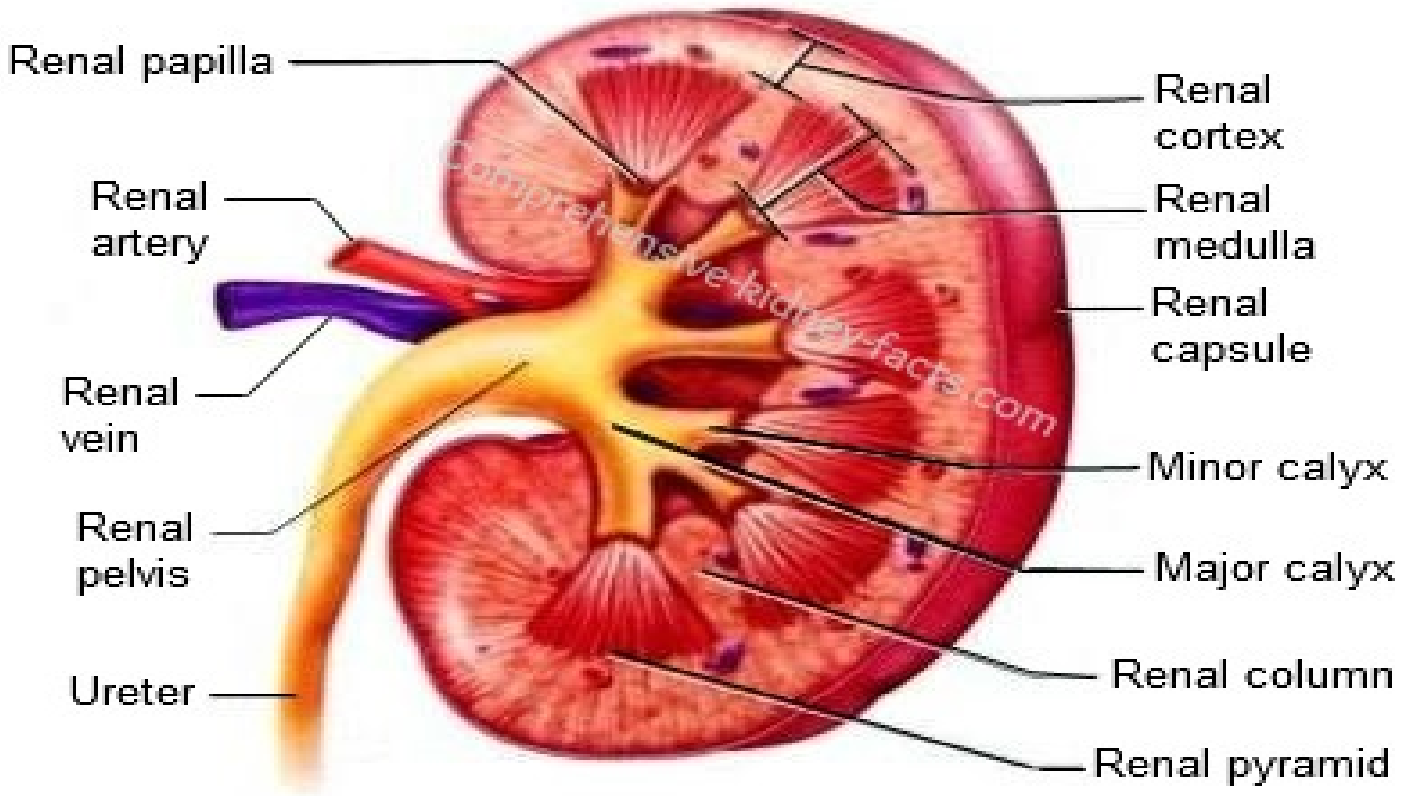

kidney
ureter
bladder
urethra
ureter

EPIDIMIOLOGY OF UROTHELIAL TUMORS OF RENAL PELVIS AND URETER

- Upper urothelial cancers are rare in western countries with annual estimated incidence of 1 or 2 new cases per 100,000 inhabitants
- Risk Factors
  - Age (50-80 yrs)
  - Gender (M>F 3:1)
  - Balkan nephropathy (Albania, Bosnia, Bulgaria, Croatia...)
  - Smoking
  - Phenacetin abuse
  - Occupational factors
  - Heredity (Lynch Syndrome)


Renal papilla
Renal artery
Renal vein
Renal pelvis
Ureter
Renal cortex
Renal medulla
Renal capsule
Minor calyx
Major calyx
Renal column
Renal pyramid

LYNCH SYNDROME AND TCC

- Estimates of lifetime risk of urinary tract cancer in LS range from 0.2-25%
  - Depending of the study and which urinary tract cancers are included
  - Increased risk of urothelial cancer of upper urinary tract (renal pelvis and ureter)
- Highest risk in MSH2-mutation carriers, especially males over the age of 50-70 yrs
- Younger age of onset (typically 10-15 yrs earlier)
- Sometimes family clusters of TCC

CLINICAL PRESENTATION

- Microscopic hematuria
- Gross hematuria
- Flank pain
- Asymptomatic (10-15%)

INVESTIGATIONS

- Urinalysis
- Urine cytology
- Cystoscopy, retrograde pyelography
- Ureteroscopy
- Ultrasound
- CT
- MRI

DETECTION

- Urinary dipstick
  - simplest test
  - sensitivity 91-100%
  - specificity 65-99%
  - false positives
    - myoglobin
    - free hemoglobin in urine
    - oxidizing contaminants in urine (povidine-iodine)

DETECTION

- Initial finding of microscopic hematuria on urinary dipstick should be confirmed by microscopic evaluation of urinary sediment
- Limitation in screening
  - Not specific to urinary tract cancer
  - Can be seen with many other urological conditions, including kidney stones, infections, inflammation…

URINE CYTOLOGY

- performed on urothelial cells routinely exfoliated into urine
- voided specimen vs bladder wash specimen
- sensitivity of voided cytology 40-76%
- depends on # specimens examined, stage/grade of bladder tumor, expertise of cytopathologist

URINE CYTOLOGY

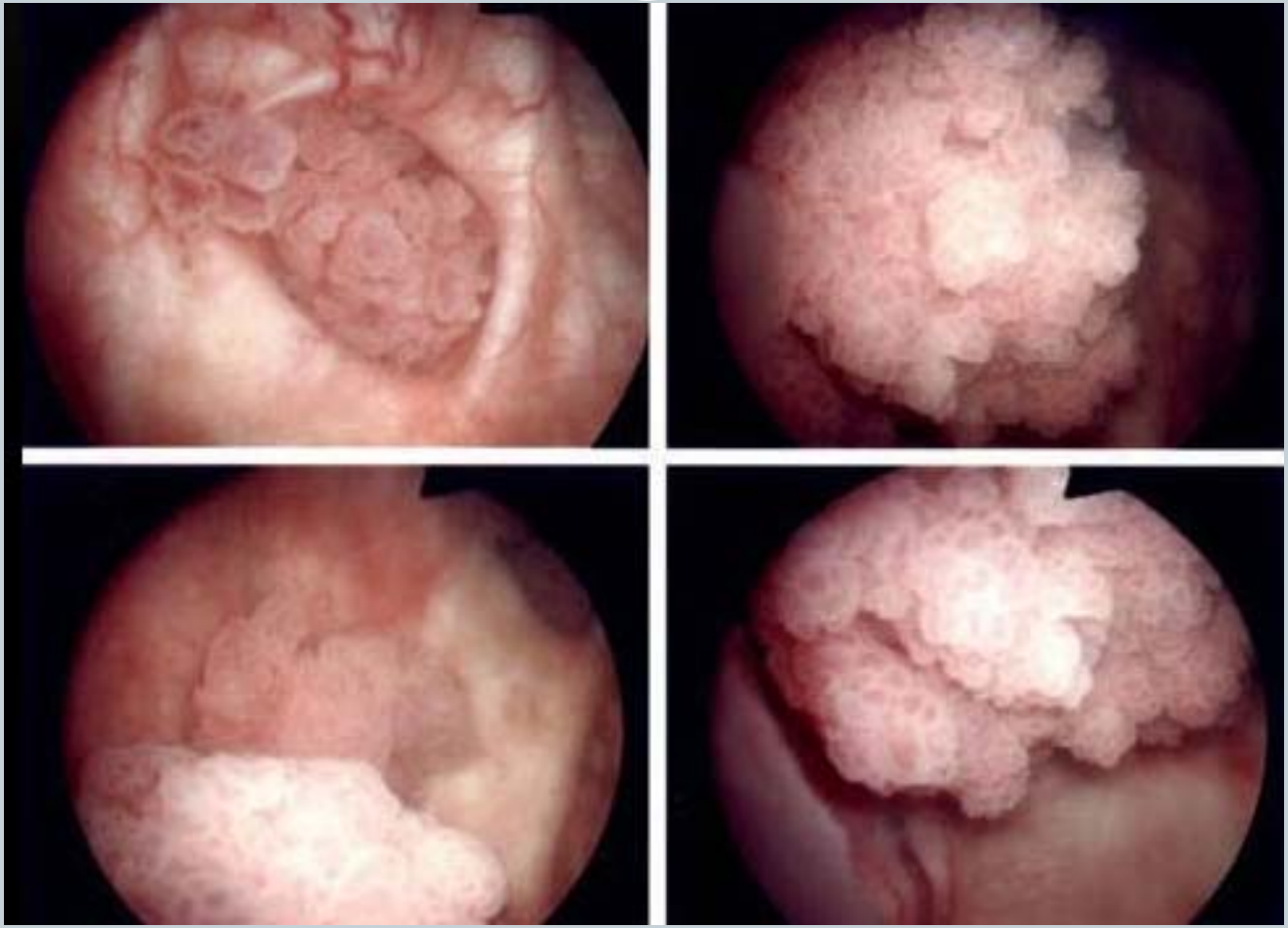
- Positive cytology → virtually diagnostic of UTC
- Negative cytology → less helpful (high incidence FN) → exclude high-grade tumors
- Atypical, suspicious cytology
  - only 15% with atypical/suspicious cytology have underlying urinary tract malignancy
- Limitation in screening
  - Very low sensitivity
  - Many false positive results

CYSTOSCOPY

- Allows complete visualization of bladder mucosa, urethra
- Flexible vs rigid
- Limitation as screening procedure
  - Invasive
  - Expensive
  - Patient discomfort
  - Potential for UTI

CYSTOSCOPY

UROTHELIAL CANCER



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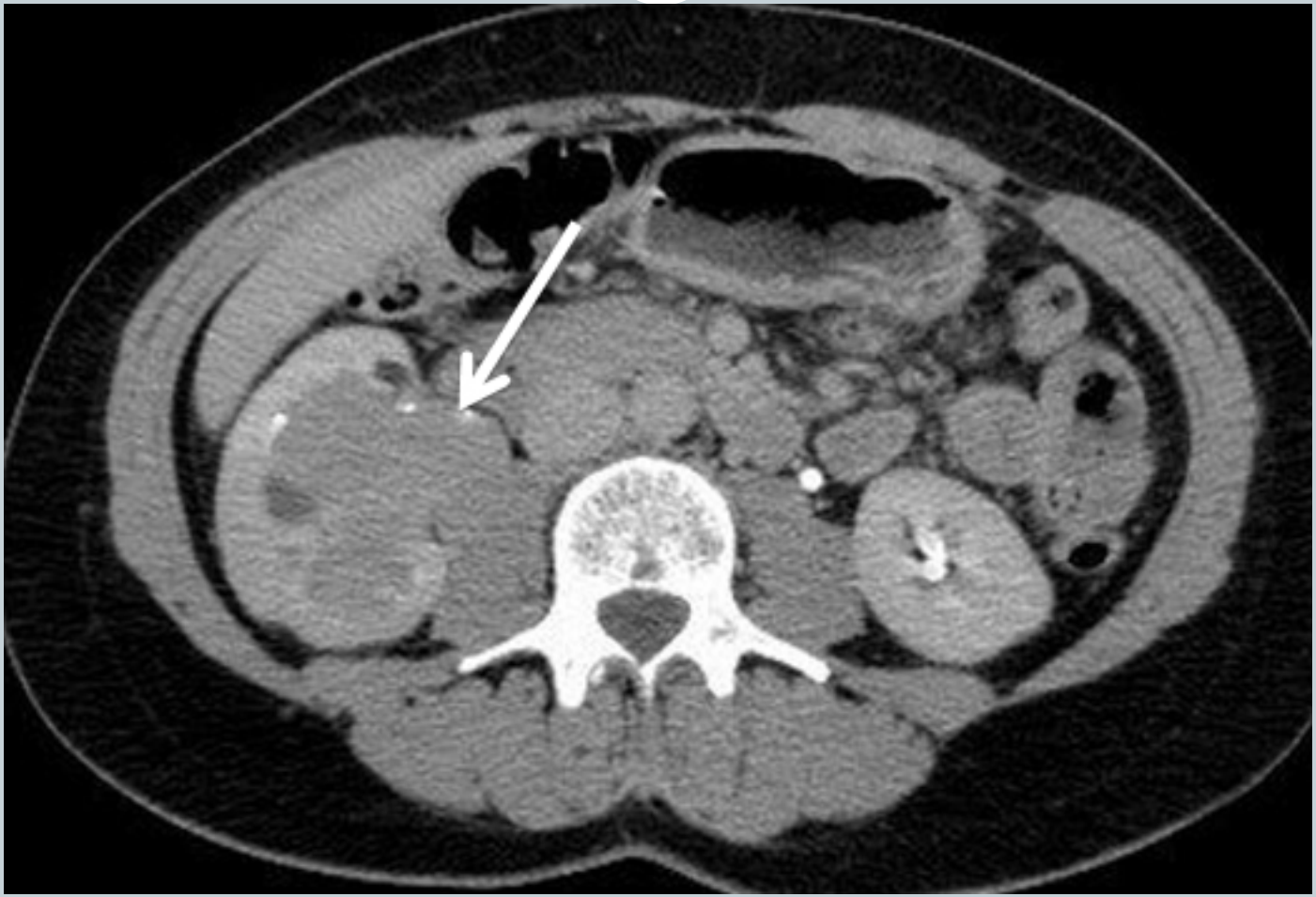
IMAGING

- **U/S**
  - Excellent for detection, characterization of renal cysts
  - Not very accurate for diagnosing small urinary tract cancers especially in renal pelvis, ureter
  - Not invasive
  - No radiation exposure

IMAGING

- **C/T**
  - best modality for evaluation solid renal masses, stones, infection
  - Involves non-contrast, contrast and delayed images
  - Small <1cm tumors may not be visualized
  - Limitation in screening
    - Risk of radiation, esp. if repeated studies and risk of subsequent cancer

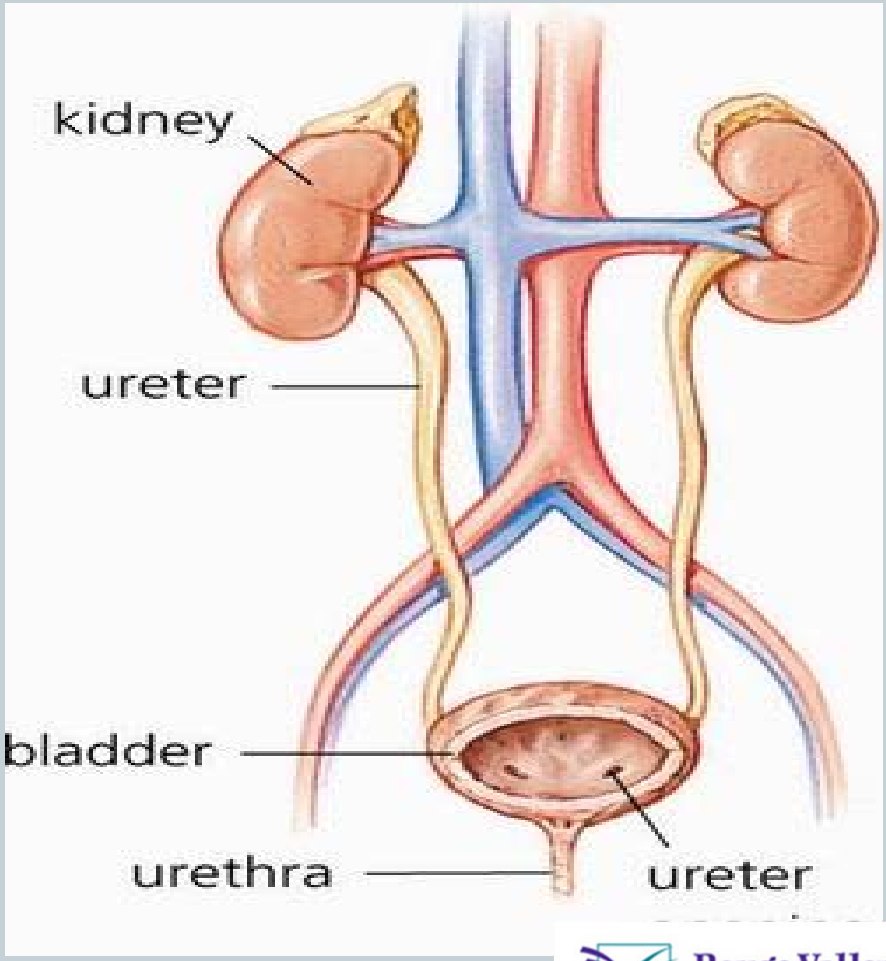


IMAGING

- **MRI**
  - similar detection rates of renal masses compared to CT
  - more expensive
  - limited availability
  - used as problem-solving approach after CT, u/s

TREATMENT

- Varies depending on location of tumor
- Renal Pelvis and Upper Ureter
  - Radical nephro-ureterectomy
  - Percutaneous resection
  - Laser ablation
- Mid Ureter
  - Segmental resection
- Distal Ureter
  - Distal ureterectomy and reimplantation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SCREENING - GENERAL

- Disease is common, high morbidity and mortality
- Treatment modalities are acceptable, safe and relatively inexpensive
- Aims to insure that as few as possible with disease get through undetected (high sensitivity)
- As few as possible without disease should be subject to further investigation (high specificity)
- High likelihood a positive screening will give a correct result (positive predictive value)

SCREENING – BLADDER CANCER

- Screening has not been shown to be effective with urine cytology and urinalysis for microscopic hematuria for urinary cancer in the general population and in groups at higher risk for bladder cancer from environmental factors
- Benefit of ultrasound screening is unknown

SCREENING AND LYNCH SYNDROME

- 2 studies have looked at systematic screening
  - Denmark used urine cytology
    - Sensitivity of diagnosing asymptomatic UTC only 29%
    - 0.1% of examinations lead to detection of asymptomatic UTC
    - High false positive leading to unnecessary invasive procedures
    - "Urine cytology is not an appropriate screening method"
  - 1 initial CT, biannual cystoscopy and urine cytology
    - "Evidence for systematically screening in LS is lacking"
    - "Need for further investigation to find optimal screening methods and population to offer screening"

SCREENING AND LYNCH SYNDROME

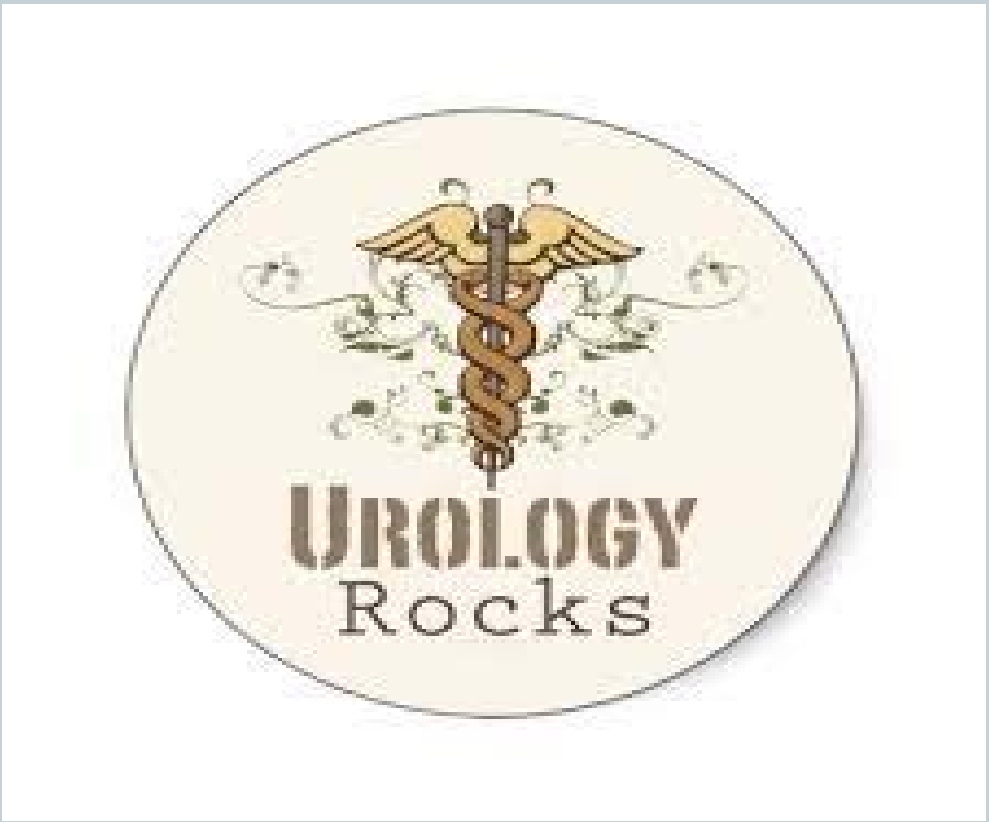
- Neither study able to answer question of whether screening for UTC in LS is recommendable
- No standard screening recommendations have been established internationally
- Mallorca group
  - If two or more cases of UTC in family
    - Urinalysis, urine cytology
    - Annual/biennial ultrasound from age 30-35 yrs

SCREENING AND LYNCH SYNDROME

- Risk stratification approach
  - Low risk with no personal or family history of UTC and no MSH2-mutation
    - Offer annual urinalysis and urine cytology
  - Intermediate risk with family history of UTC or MSH2-mutation
    - Offer annual urinalysis, urine cytology and ultrasound
  - High risk with personal history of UTC
    - Offer annual urinalysis, urine cytology, CT and cystoscopy

MT. SINAI GENETIC CLINIC

- "There are non-invasive screenings, such as urinalysis (looking for microscopic traces of blood in the urine) and urine cytology, but it has been known to miss cancers or it may falsely identify problems that lead to more invasive and unnecessary procedures.
- More invasive screening, such as cystoscopy is not routinely recommended for Lynch syndrome families.
- Screening recommendations are not evidence-based or known to be completely effective, however, **we would suggest that you speak with your family doctor about doing yearly urinalysis and urine cytology using 2 different urine samples.**
- These recommendations may change in the future and you are also welcome to contact us periodically for updates."



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