GRAND ROUNDS CLINICI DEL MERCOLEDÌ
con il Policlinico San Matteo

Sistema Socio Sanitario
Regione Lombardia

Fondazione IRCCS Policlinico San Matteo

ATS Pavia

Aula Magna "C. Golgi"
& WEBINAR

08/03/2023

Richard Naspro

Tumore delle alte vie urinarie: difficoltà in un management multidisciplinare complesso

Dati anamnestici (Gennaio 2017)

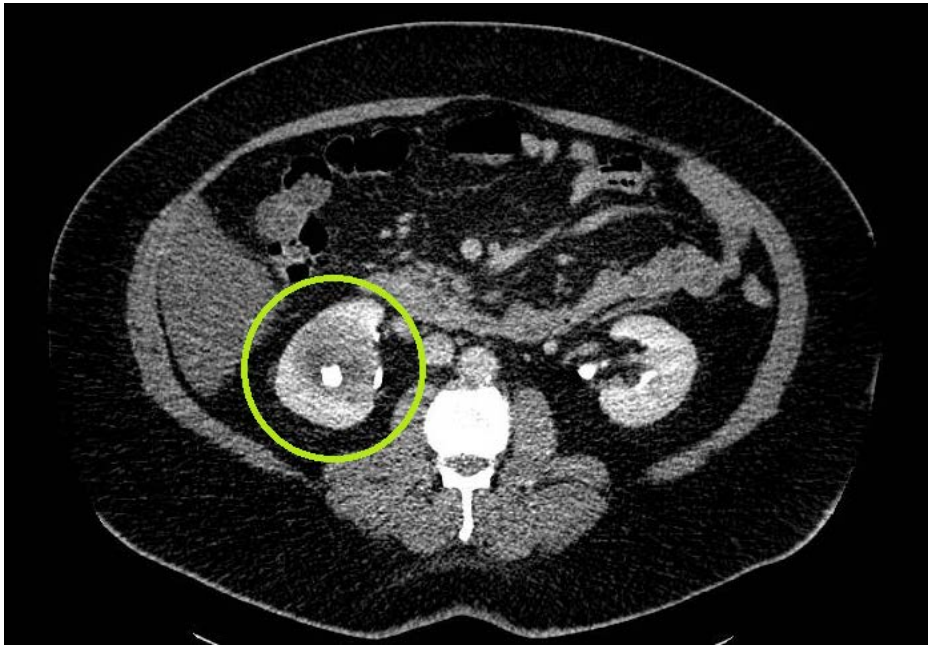
- Età: 60 anni, **BMI = 56.6 kg/m^2** (**Obese Class III**), non totale compliance

- APP: durante controllo diabetologico ha eseguito TC addome con riscontro di lesione renale dubbia (probabile flogosi renale), da qualche settimana franca ematuria

- APR: obesità patologica, ipertensione arteriosa, diabete mellito 2, iperuricemia, ipotiroidismo, appendicectomia

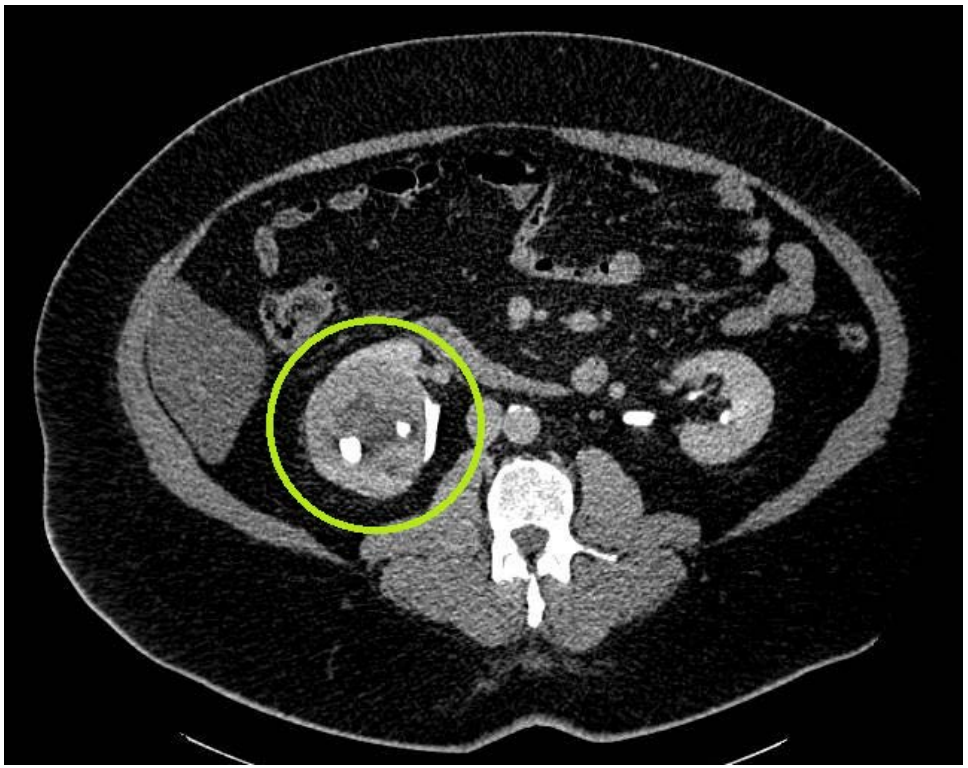
TC addome 23/02/2017

- Formazione tondeggiante di circa 48-49 mm, a struttura inomogenea, al terzo medio-superiore del rene destro, attribuibile a formazione ascessuale
- Normalità del rene di sinistra senza formazioni patologiche
- Non linfoadenomegalie addomino-pelviche
- Vescica poco distesa a pareti regolari senza lesioni infiltranti o aggettanti



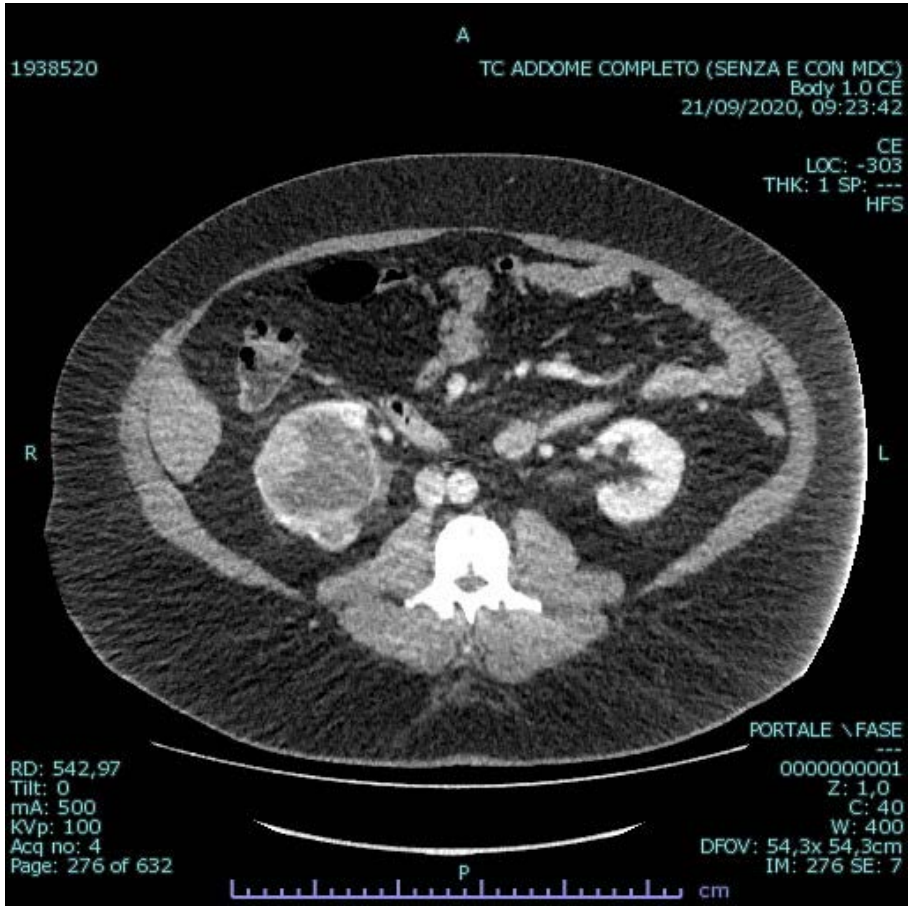
TC addome 12/09/2018

- Invariata per morfologia e dimensioni la formazione ascessuale tondeggiante del rene di destra (48-49 mm), più omogenea
- Porzione centrale ipodensa con pareti ispessite e lieve impregnazione contrastografica.
- Non linfoadenomegalie addomino-pelviche



TC addome 21/09/2020

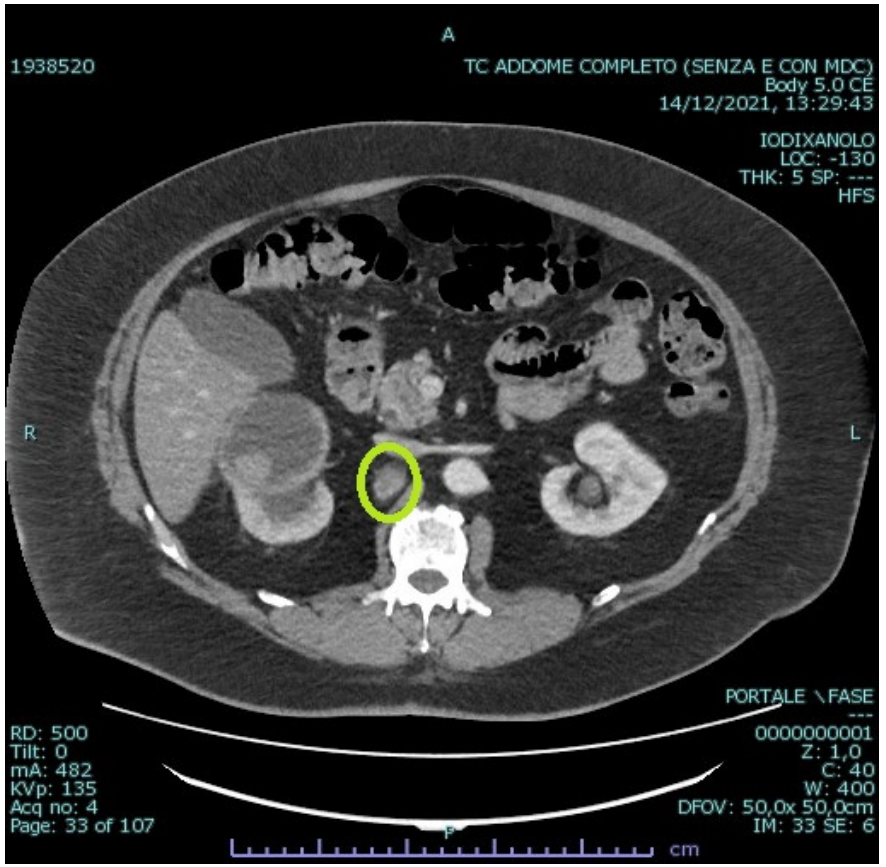
- Aumento dimensioni lesione renale (76x67 mm), ispessita la parete infero laterale (14 mm) e dotata di arricchimento contrastografico
- Non linfoadenomegalie addominali (a posteriori linfonodi sovra e sotto renali dubbi ma non sicuramente sospetti in senso oncologico)
- Invariato il resto (non lesioni in vescica)



TC addome 14/12/2021

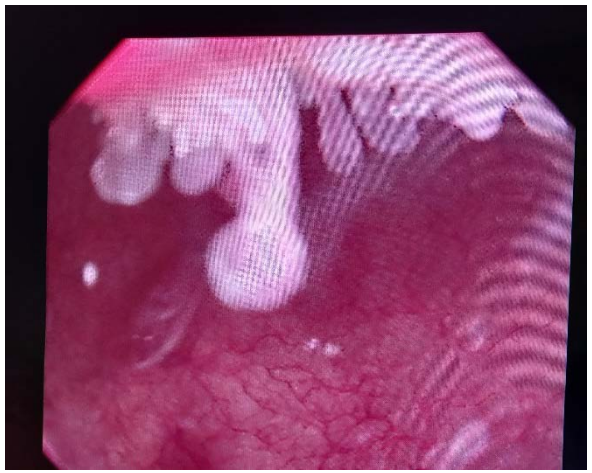
Accesso in PS in data 06/12/2021 per ematuria e ritenzione urinaria

- Lesione renale aumentata di dimensioni (91 x 78 mm)
- In vescica due formazioni polipoidi di 20 mm e 13 mm
- Non linfoadenopatie (a posteriori aumento numerico e volumetrico di linfonodi, sovra e sottorenali, il maggiore sovrarenale di 18 x 15 mm, sospetto. Più piccoli linfonodi in sede sottorenale fino al Carrefour, inferiori ai 5 mm, ma dubbi/sospetti)



TURBT + Ureterorenoscopia destra 16/12/2021

- Vescica: Lesione papillare di circa 3 cm a livello della parete postero-laterale sinistra e una analoga a livello della parete postero-superiore/cupola di difficile raggiungimento
- Pelvi renale destra completamente occupata da tessuto papillare verosimilmente neoplastico, sanguinante



TURBT 16/12/2021

Esame istologico (30/12/2021)

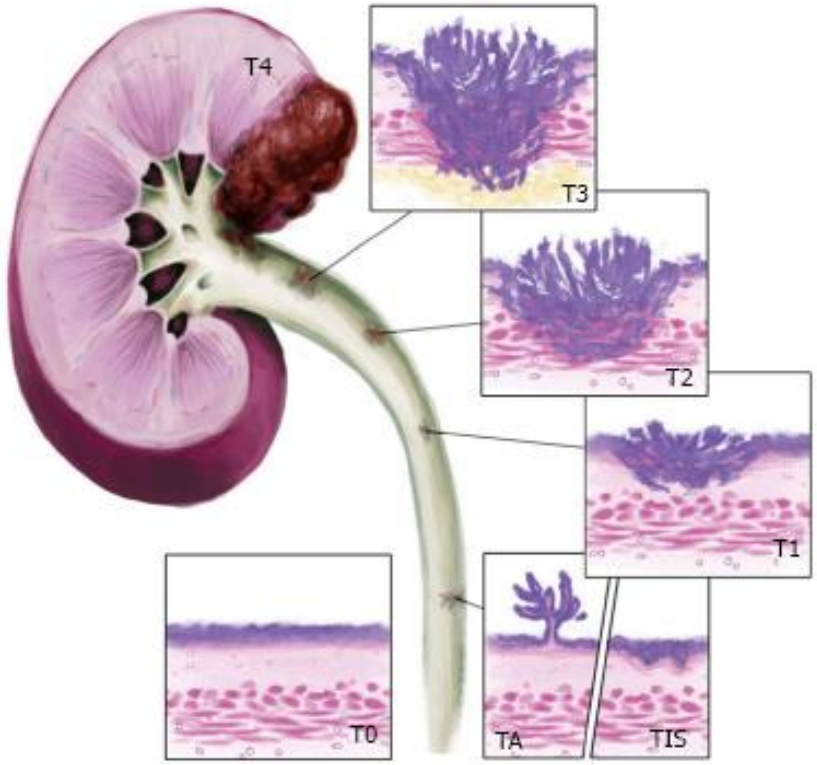
- Neoformazione vescicale: carcinoma uroteliale ad alto grado, G2
- Base impianto: alterazioni da elettrocuzione, indenne da neoplasia
- Neoformazione pelvi renale dx: Il contenitore pervenuto contiene esclusivamente liquido fissativo

Epidemiology

Upper urinary tract UCs are uncommon and account for only 5–10% of UCs

Annual incidence two cases per 100,000 inhabitants.

Pyelocaliceal tumours are approximately twice as common as ureteral tumours and multifocal tumours are found in approximately 10–20% of cases



The 5-year survival rates of T1, T2, T3, and T4 patients were 90.2%, 78%, 43.8%, and 18.5%, respectively.

EAU Guidelines on

Upper Urinary Tract Urothelial Carcinoma

M. Rouprêt, M. Babjuk (Chair), M. Burger (Vice-chair),
E. Compérat, N.C. Cowan, P. Gontero, F. Liedberg,
A. Masson-Lecomte, A.H. Mostafid, J. Palou,
B.W.G. van Rhijn, S.F. Shariat, R. Sylvester
Guidelines Associates: O. Capoun, D. Cohen,
J.L. Dominguez-Escrig, T. Seisen, V. Soukup

European Association of Urology

NCCN National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Bladder Cancer

Version 3.2021 — April 22, 2021

NCCN.org

NCCN Guidelines for Patients® available at www.nccn.org/patients

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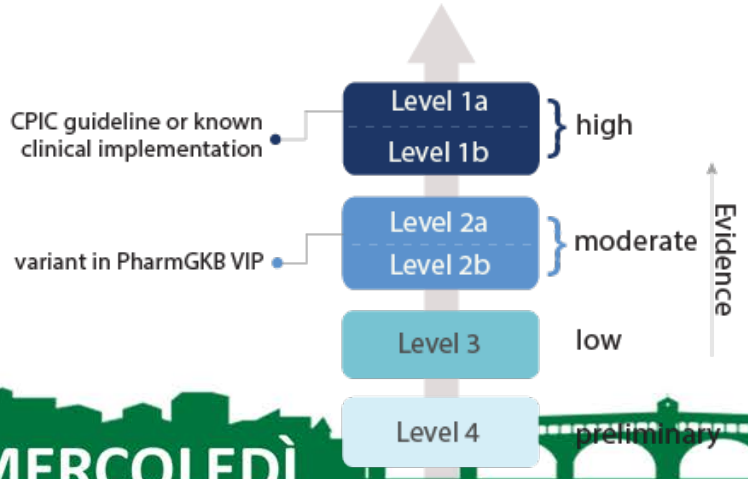
6.4 Summary of evidence and guidelines for the prognosis of UTUC

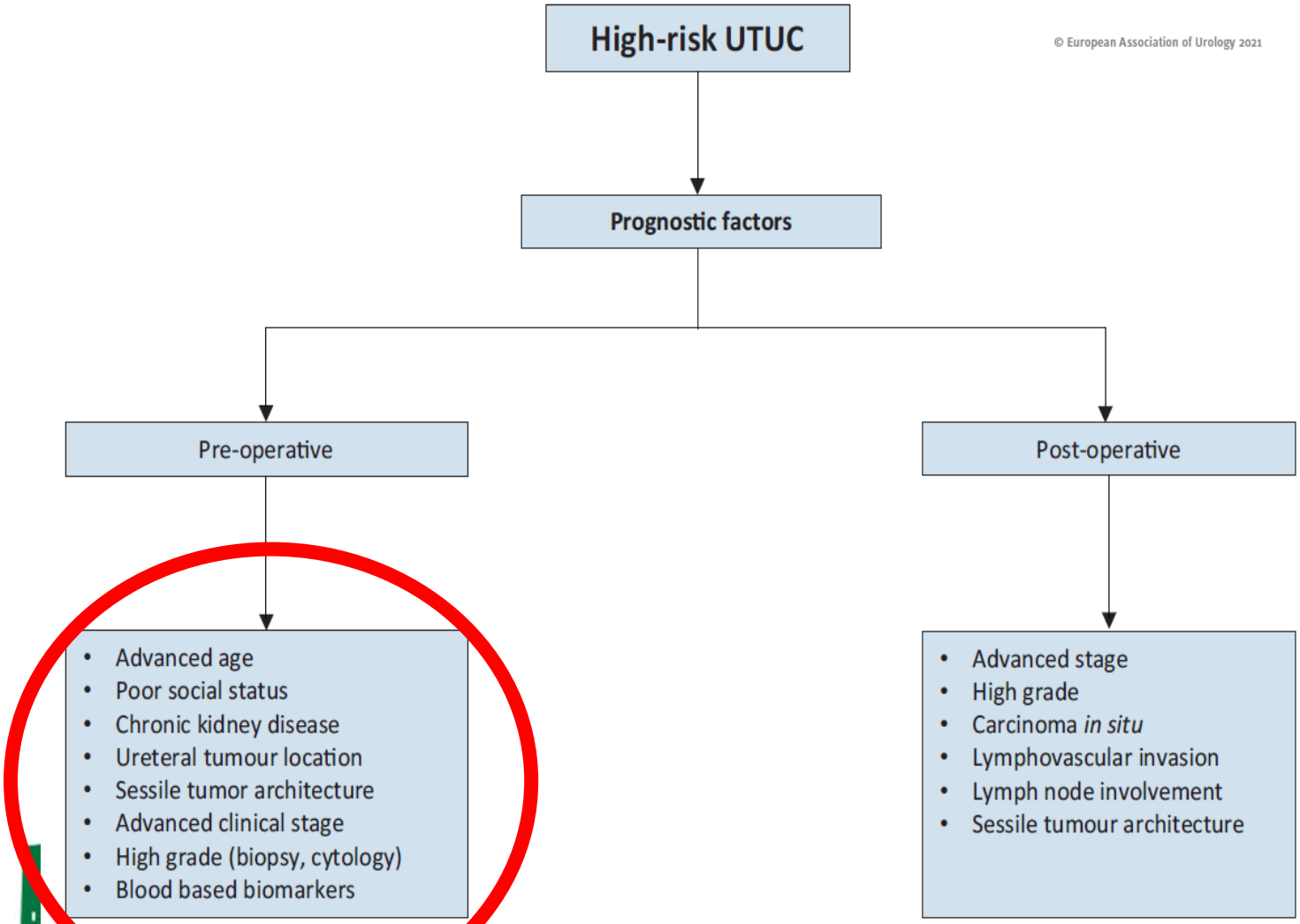
Summary of evidence	LE
Important prognostic factors for risk stratification include tumour multifocality, size, stage, grade, hydronephrosis and variant histology.	3
Models are available to predict non-organ confined disease and altered prognosis after RNU.	3
Patient, tumour and treatment-related factors impact risk of bladder recurrence.	3
Currently, no prognostic biomarkers are validated for clinical use.	3

Recommendation	Strength rating
Use prognostic factors to risk-stratify patients for therapeutic guidance.	Weak

Low level of evidence….



Upper Urinary tract urothelial cell carcinoma: prognostic factors included in prognostic models



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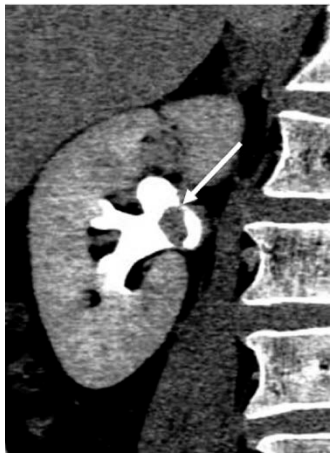
Risk stratification for UTUC according to the European Association of Urology

Explore the EAU guidelines[1]

Patient has ALL of the following
Unifocal disease
Tumor size < 2 cm
Low-grade cytology
Low-grade URS biopsy
No invasive aspect on CTU

Patient has ANY of the following
Multifocal disease
Tumor size > 2 cm
High-grade cytology
High-grade URS biopsy
Hydronephrosis
Prior radical cystectomy for bladder cancer
Variant histology

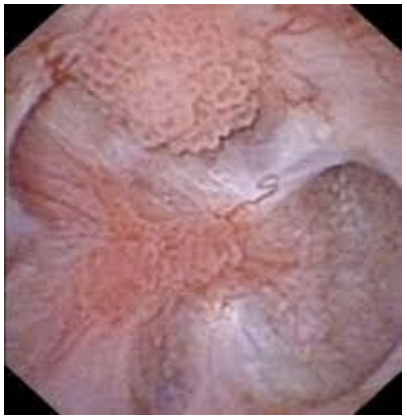
Accurate staging and grading is crucial for appropriate disease management



UTUC management should include risk-stratification of tumors to identify those more suitable for kidney-sparing approaches, without compromising oncological outcomes

Risk stratification in UTUC is primarily driven by biopsy findings

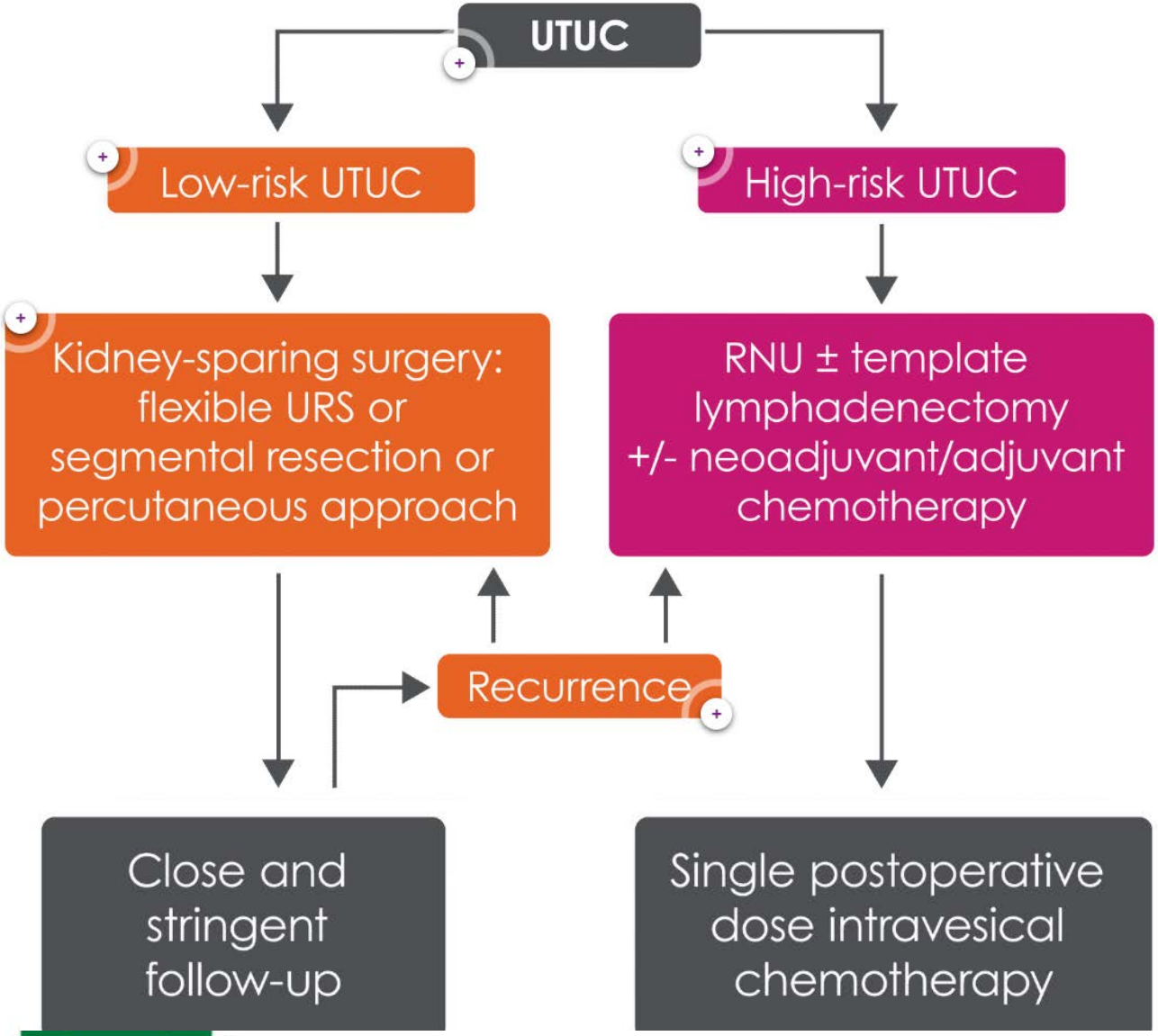
Ureteroscopic biopsy is the initial step in tissue diagnosis



Tumor grade has been shown to be correlated with muscle invasion

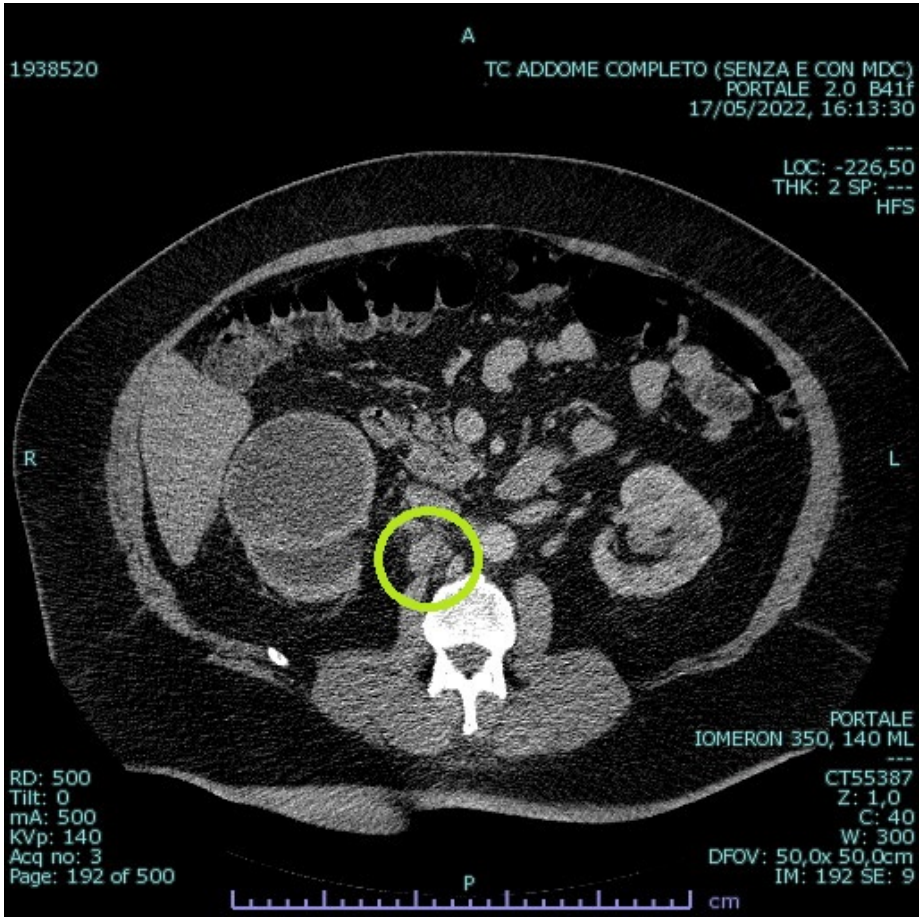
Ureteroscopy also offers the surgeon a practical, accurate evaluation of tumor location, which is useful if nephron sparing approaches are to be considered

Algorithm for UTUC treatment



TC addome 17/05/2022

- Minimo incremento dimensionale della lesione del rene di destra
- Permangono focali ispessimenti vescicali.
- **Più evidenti per numero e dimensioni le tumefazioni linfonodali localizzate a dx, in sede retrocavale**, in corrispondenza del piano passante per l'arteria renale e in sede interaorto-cavale (il maggiore di 20x16 mm).



TURBT 29/07/2022

- Parete posteriore e cupola occupati da neoformazione papillare di almeno 4.5 cm e presenza di altre lesioni papillari a livello diffuso nel viscere

- **Vista l'estensione della lesione e la difficoltà nella resezione si soprassiede dall'effettuare la ureterorenoscopia e la biopsia ureterale**

Esame istologico (08/08/2022)

- Neoformazione vescicale: carcinoma uroteliale ad alto grado, G2-G3 non muscolo infiltrante

Discussione Urologica

Si programma TURBT II look per sospetta neoplasia vescicale muscolo infiltrante e biopsia renale per staging upper tract

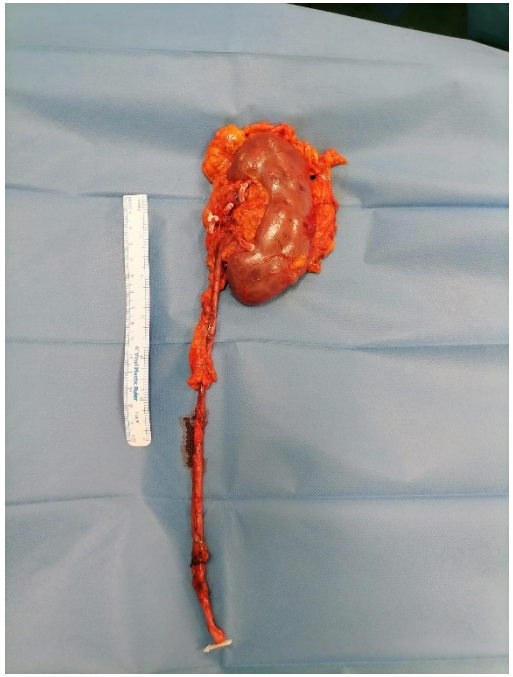
TURB 14/12/2022

- Vescica: Si individuano 4 neoformazioni papillari di circa 6 mm ciascuna, esofitiche, a livello della cupola, associate ad alcune lesioni millimetriche sulla parete posteriore
- Pelvi renale appare occupata da plurime lesioni papillari vegetanti, biopsia

- **Esame istologico (30/12/2022)**
- Neoformazione vescicale: carcinoma uroteliale papillare ad alto grado, G2-G3, focale infiltrazione della tonaca sottomucosa
- Neoformazione calice rene destro: **frammenti di mm 1 costituiti da proliferazione papillare (citocheratina 7+), suggestiva per neoplasia uroteliale, non ulteriormente qualificabile.**

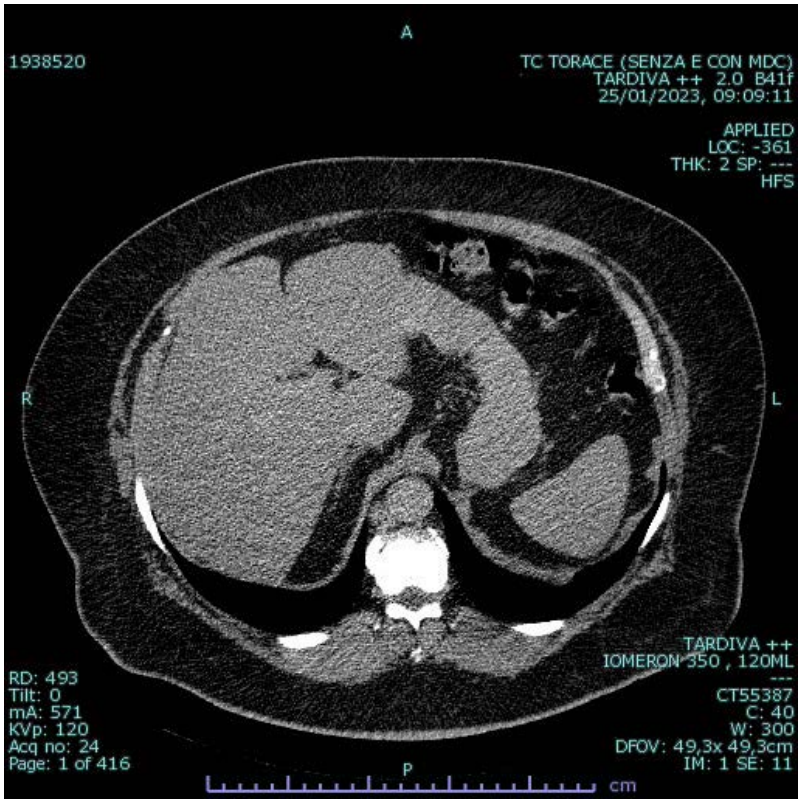
Planning

Proposto intervento di nefroureterectomia laparoscopica con pastiglia vescicale + linfoadenectomia retroperitoneale previo re-staging radiologico



TC total body 25/01/2023

- **Incremento dimensionale della massa a livello del rene destro (13cm x 10cm x 12cm)**
- **Disomogenee tumefazioni linfonodali in sede laterocervicale a sinistra, retroclaveare bilaterale, paratracheale destra, loggia di Barety e retrocurale para-aortica destra**
- **Incremento dimensionale e di numero delle tumefazioni linfonodali addominali le maggiori in sede inter-aorto-cavale, retrocavale e paracavale inferiore**
- **Plurimi linfonodi in sede otturatoria bilaterale sospetti**
- **Irregolare ispessimento della parete posteriore della vescica, con spessore fino a circa 12 mm, con impregnazione contrastografica.**



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Linee guida per malattia metastatica

Malattia metastatica (9 % dei pazienti hanno malattia metastatica alla diagnosi)	**Strength rating**
Offer radical nephroureterectomy as a palliative treatment to symptomatic patients with resectable locally advanced tumours.	Weak
First-line treatment for cisplatin-eligible patients	
Use cisplatin-containing combination chemotherapy with GC or HD-MVAC.	Strong
Do not offer carboplatin or non-platinum combination chemotherapy.	Strong
Use maintenance avelumab in patients who did not have disease progression after 4 to 6 cycles of gemcitabine plus cisplatin.	Strong
First-line treatment in patients unfit for cisplatin	
Offer checkpoint inhibitors pembrolizumab or atezolizumab depending on PD-L1 status.	Weak
Offer carboplatin combination chemotherapy if PD-L1 is negative.	Strong
Use maintenance avelumab in patients who did not have disease progression after 4 to 6 cycles of gemcitabine plus carboplatin.	Strong
Second-line treatment	
Offer checkpoint inhibitor (pembrolizumab) to patients with disease progression during or after platinum-based combination chemotherapy for metastatic disease.	Strong

Radiological staging

Summary of evidence	LE
The diagnosis and staging of UTUC is best done with computed tomography urography and URS.	2a
Selective urinary cytology has high sensitivity in high-grade tumours, including carcinoma *in situ*.	3
Urethrocystoscopy can detect concomitant BC.	2a

Recommendations	Strength rating
Perform a urethrocystoscopy to rule out bladder tumour.	Strong
Perform a computed tomography (CT) urography for diagnosis and staging.	Strong
Use diagnostic ureteroscopy (preferably without biopsy) if imaging and/or voided urine cytology are not sufficient for the diagnosis and/or risk-stratification of patients suspected to have UTUC.	Strong
Magnetic resonance urography or ^{18}F-Fluorodeoxglucose positron emission tomography/CT (to assess [nodal] metastasis) may be used when CT is contra-indicated.	Weak

UPDATES

Recommendations	Strength rating
2022 recommendation: Use diagnostic ureteroscopy and biopsy if imaging and cytology are not sufficient for the diagnosis and/or risk-stratification of the tumour.	Strong
Revised 2023 recommendation: Use diagnostic ureteroscopy (preferably without biopsy) if imaging and/or voided urine cytology are not sufficient for the diagnosis and/or risk-stratification of patients suspected to have UTUC.	Strong
2022 recommendation: Magnetic resonance urography or ^{18}F-Fluorodeoxglucose positron emission tomography/CT may be used when CT is contra-indicated.	Weak
Revised 2023 recommendation: Magnetic resonance urography or ^{18}F-Fluorodeoxglucose positron emission tomography/CT (to assess [nodal] metastasis) may be used when CT is contra-indicated.	Weak

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Take Home Messages

- UTUC = always Challenging cases
- Necessità di anticipare il tempo della discussione multidisciplinare (Radiologi-Oncologi-Medico nucleare...)
- Considerare alternative alla TC nello staging linfonodale e metastatico in casi selezionati