

PMCC Dialogue 2019

Role of Transplant Surgeon in Renal Malignancy Care – Nephron-sparing Options

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Division of Urology

Conflicts of Interest

- NO relevant disclosures

Learning Objectives

- advantages & disadvantages of ex-vivo NSS with renal auto-transplantation
- indications/contraindications to ex-vivo NSS with renal auto-transplantation

Case #1

- 57yo male with incidental left RCC
 - 4.2cm endophytic, no mets
- PMHx
 - right Nx as teen for MVA trauma
 - DM, HTN, GERD, psoriasis
- Labs
 - creat 126, stable for past few years
 - u/a demonstrates trace RBC, protein
 - Bx shows ccRCC F2



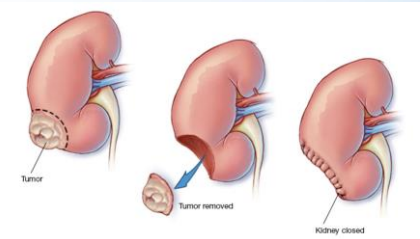
Case #1

- Radical Nx + HD
- PNx +/- HD
- Thermal-ablation
- other



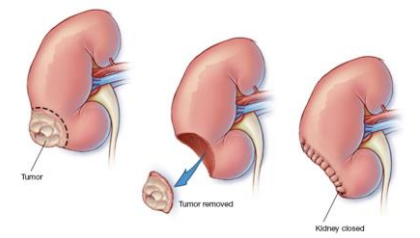
Renal Cell Carcinoma

- Indications for NSS for RCC
 - solitary kidney
 - RCC in CKD pt
 - bilateral RCC
 - RCC in genetic syndrome pt (eg VHL, etc)
 - RCC with renal risk factors (eg DM, HTN, RAS, etc)
 - elective NSS (eg cT1a)



Renal Cell Carcinoma

- Indications for NSS for RCC
 - **solitary kidney***
 - **RCC in CKD pt***
 - bilateral RCC
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 - RCC with renal risk factors (eg DM, HTN, RAS, etc)
 - elective NSS (eg cT1a)



ex-vivo NSS + Auto-Tx for RCC

- advantages

- extirpation in bloodless field
- reduced parenchymal resection
- lower EBL, ability to “test” renorrhaphy
- shorter WIT
- avoid ESRD
- oncologically comparable to RN, ?superior to thermal-ablation

- disadvantages

- longer OR time
- longer overall ischemia (CIT+WIT)
- increased morbidity
- potential vascular complications

Oncology: Adrenal/Renal/Upper Tract/Bladder

Open Partial Nephrectomy for Tumor in a Solitary Kidney: Experience With 400 Cases

Amr F. Fergany,* Ismail R. Saad, Lynn Woo and Andrew C. Novick

From the Glickman Urological Institute, Cleveland Clinic Foundation, Cleveland, Ohio

- 400 patients with RCC in solitary kidney
- 5yr CSS 89% (incl 38% \geq T2)
- 2 patients (0.5%) required immediate HD
 - mean pre-op creat 1.4 mg/dL
- 18 pts (4.5%) progressed to HD
 - mean 3.6yrs after OR

RENAL CELL CARCINOMA IN THE SOLITARY KIDNEY: AN ANALYSIS OF COMPLICATIONS AND OUTCOME AFTER NEPHRON SPARING SURGERY

REZA GHAVAMIAN*, JOHN C. CHEVILLE, CHRISTINE M. LOHSE, AMY L. WEAVER,
HORST ZINCKE AND MICHAEL L. BLUTE

- 63 patients } 90% prior RNx, 10% congenital
- 55 PNx, 8 ex-vivo PNx + KAT
- 5yr CSS 80.7% (incl 11% ≥T2)
- temporary HD in only 1 pt

TABLE 3. Associations with death from any cause

Feature	Univariate	
	Risk Ratio (95% CI)	p Value
Age at surgery	1.34 (0.90–1.99)*	0.153
Male gender	1.31 (0.59–2.91)	0.514
Tumor size	2.06 (0.99–4.30)†	0.054
Tumor size 5 cm. or greater	1.49 (0.72–3.11)	0.287
Tumor stage pT3b or pT4	9.17 (2.85–29.55)	<0.001
Nuclear grade 3	3.48 (1.49–8.09)	0.004
Multifocality	1.14 (0.50–2.60)	0.756
Clear cell subtype	1.72 (0.49–6.01)‡	0.398
Partial nephrectomy	1.04 (0.50–2.20)	0.911
Enucleation	0.93 (0.44–1.96)	0.84

For tumor stage pT3b or pT4 and nuclear grade 3 multivariate risk ratio 6.76 (95% CI 1.90 to 24.02), p = 0.003 and 2.54 (95% CI 1.01 to 6.39), p = 0.048, respectively.

TABLE 4. Associations with death from renal cell carcinoma

Feature	Univariate	
	Risk Ratio (95% CI)	p Value
Age at surgery	1.06 (0.67–1.68)*	0.808
Male gender	1.33 (0.47–3.76)	0.588
Tumor size	2.88 (1.15–7.21)†	0.024
Tumor size 5 cm. or greater	2.09 (0.82–5.31)	0.121
Tumor stage pT3b or pT4	10.73 (2.74–42.03)	<0.001
Nuclear grade 3	4.60 (1.77–11.92)	0.002
Multifocality	1.22 (0.43–3.44)	0.706
Partial nephrectomy	1.12 (0.44–2.85)	0.806
Enucleation	0.84 (0.33–2.15)	0.722

For tumor stage pT3b or pT4 and nuclear grade 3 multivariate risk ratio 5.63 (95% CI 1.31 to 24.17) and 3.45 (95% CI 1.22 to 9.75), p = 0.02, respectively.

ex-vivo NSS + Auto-Tx for RCC

- Indications

- solitary kidney or advanced CKD pt
- thermal-ablation not recommended/not technically feasible

AND

- higher stage, RENAL nephrometry/PADUA score
- complex renal anatomy (eg pelvic kidney, prior renal surgery, etc)
- multifocal RCC

*** significant EBL and prolonged WIT expected ***

ex-vivo NSS + Auto-Tx for RCC

- **Contraindications**

- high grade, aggressive variants
- expected residual renal mass <33%
- eGFR <30mL/min (ie \geq stage 4 CKD)
- progressively declining renal function with ++ renal risk factors (m-CKD)
- anatomic considerations (eg R kidney with short RV, ≥ 3 arteries, calcified pelvic vessels, etc)

The Role of Renal Autotransplantation in Complex Urological Reconstruction

Andrew C. Novick , Charles L. Jackson, Ralph A. Straffon

- 108 pts } 14 patients w/ RCC
 - solitary kidney or B/L RCC
- 4 of 14 developed recurrence/mets (29%)
 - 3 (21%) had concurrent mets, 8 (57%) with T1 RCC
- 2 of 14 required RRT (14%)
 - >2/3 of kidney removed in both cases

Kidney autotransplantation after nephrectomy and work bench surgery as an ultimate approach to nephron-sparing surgery

Martin W. W. Janssen^{1*}, Johannes Linxweiler¹, Ines Philipps¹, Zentia Bütow^{1,2}, Stefan Siemer¹, Michael Stöckle¹ and Carsten-Henning Ohlmann¹

- 12 patients with solitary kidney
- **5 RCC**, 5 UTUC, 1 nephroblastoma, 1 met
- 3 required HD (25%)
 - 2 temp
 - 1 permanent (8%)

ex-vivo NSS + Auto-Tx for RCC

- ?comparable oncologic outcomes
- ?improved ability to prevent need for RRT
- ?increased morbidity cf other NSS options

Case #2

- 63yo male with Lynch syndrome
 - presented with AKI (creat 300s) requiring urgent stent
- PMHx
 - R hemicolectomy 10yrs ago for ColonCa
 - left NephroU 8yrs ago for T1HG
 - few TaLG bladder recurrences since
 - HTN, GERD, CAD, remote appy, diverticulosis
- Labs
 - creat 105, stable
 - u/a demonstrates large RBCs
 - cytology -ve

Case #2



- URS Bx – LG UTUC

Case #2

- NephroU + HD +/- systemic Rx
- Segmental resection + reconstruction
- Endoscopic management
- NAC + restage
- other



UTUC

TABLE 58-3 Literature Review of Overall Survival of Patients with Upper Tract Urothelial Tumors (Renal Pelvis or Ureter) by Stage and Grade

	5-YEAR SURVIVAL (%)
TUMOR GRADE	
1-2	40-87
3-4	0-33
TNM STAGE	
Ta, T1, Tcis	60-90
T2	43-75
T3	16-33
T4	0-5
N+	0-4
M+	0

NSS for UTUC

BJU Int. 2014 August ; 114(2): 216–220. doi:10.1111/bju.12341.

Nephron Sparing Management versus Radical Nephroureterectomy for Low or Moderate Grade, Low Stage Upper Tract Urothelial Carcinoma

Jay Simhan¹, Marc C. Smaldone¹, Brian L. Egleston², Daniel Canter³, Steven N. Sterious¹, Anthony T. Corcoran¹, Serge Ginzburg¹, Robert G. Uzzo¹, and Alexander Kutikov¹

¹Division of Urologic Oncology, Department of Surgical Oncology, Fox Chase Cancer Center, Temple University School of Medicine, Philadelphia, PA 19111

²Department of Biostatistics, Fox Chase Cancer Center, Philadelphia, PA 19111

³Department of Urology, Emory University School of Medicine, Atlanta, GA 30322

Review – Urothelial Cancer

Oncologic Outcomes of Kidney-sparing Surgery Versus Radical Nephroureterectomy for Upper Tract Urothelial Carcinoma: A Systematic Review by the EAU Non-muscle Invasive Bladder Cancer Guidelines Panel

Thomas Seisen^{a,*}, Benoit Peyronnet^b, Jose Luis Dominguez-Escrig^c, Harman M. Bruins^d, Cathy Yuhong Yuan^e, Marko Babjuk^f, Andreas Böhle^g, Maximilian Burger^h, Eva M. Compératⁱ, Nigel C. Cowan^j, Eero Kaasinen^k, Joan Palou^l, Bas W.G. van Rhijn^m, Richard J. Sylvesterⁿ, Richard Zigeuner^o, Shahrokh F. Shariat^p, Morgan Rouprêt^a

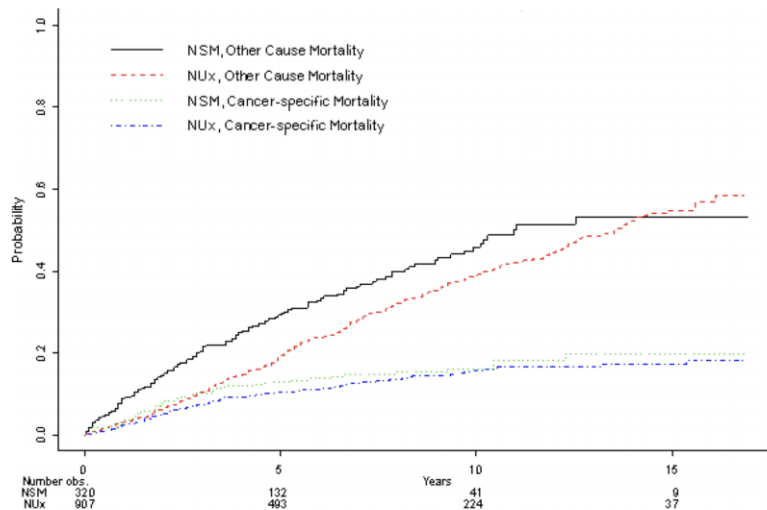


Figure 1.

- similar CSS between SU and RNU
- similar CSS between endoscopic Rx and RNU, for LG, non-invasive UTUC

NSS for UTUC

ORIGINAL ARTICLE

Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization

Alan S. Go, M.D., Glenn M. Chertow, M.D., M.P.H., Dongjie Fan, M.S.P.H., Charles E. McCulloch, Ph.D., and Chi-yuan Hsu, M.D.

What Is the Cost of Maintaining a Kidney in Upper-Tract Transitional-Cell Carcinoma? An Objective Analysis of Cost and Survival

Raymond W. Pak, M.D., Eric J. Moskowitz, and Demetrius H. Bagley, M.D.

Table 2. Adjusted Hazard Ratio for Death from Any Cause, Cardiovascular Events, and Hospitalization among 1,120,295 Ambulatory Adults, According to the Estimated GFR.*

Estimated GFR	Death from Any Cause	Any Cardiovascular Event	Any Hospitalization
	<i>adjusted hazard ratio (95 percent confidence interval)</i>		
≥60 ml/min/1.73 m ² †	1.00	1.00	1.00
45–59 ml/min/1.73 m ²	1.2 (1.1–1.2)	1.4 (1.4–1.5)	1.1 (1.1–1.1)
30–44 ml/min/1.73 m ²	1.8 (1.7–1.9)	2.0 (1.9–2.1)	1.5 (1.5–1.5)
15–29 ml/min/1.73 m ²	3.2 (3.1–3.4)	2.8 (2.6–2.9)	2.1 (2.0–2.2)
<15 ml/min/1.73 m ²	5.9 (5.4–6.5)	3.4 (3.1–3.8)	3.1 (3.0–3.3)

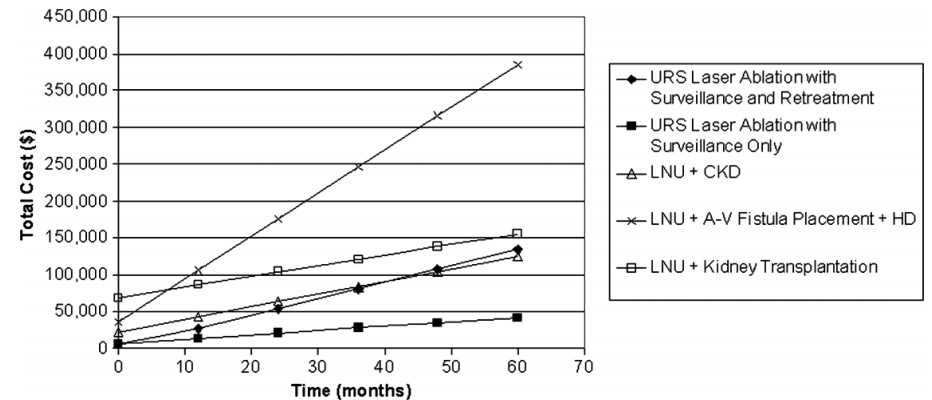


FIG. 2. Projected cost over 5 years.

Upper Tract Urothelial Ca

- Indications for NSS for UTUC
 - solitary kidney
 - UTUC in CKD pt
 - bilateral UTUC
 - UTUC in genetic syndrome pt (eg HNPCC)
 - UTUC with renal risk factors (eg DM, HTN, RAS, etc)
 - elective NSS (low-grade, low-stage disease)

ex-vivo NSS + Auto-Tx for UTUC

- advantages

- extirpation in bloodless field
- reduced risk of tumour spillage
- ?better oncologic outcomes cf endoscopic options
- avoid ESRD
- ability to administer adjuvant nephrotoxic meds
- can easily survey upper tract
- ?more effective delivery of topical adjuvants

ex-vivo NSS + Auto-Tx for UTUC

- disadvantages
 - worse oncologic outcomes cf nephroU*
 - margin status issues
 - increased morbidity
 - potential vascular complications

PARTIAL NEPHRECTOMY FOR RENAL UROTHELIAL TUMORS: CLINICAL UPDATE

MAHESH C. GOEL, SURENA F. MATIN, ITHAAR DERWEESH, HOWARD LEVIN,
STEVAN STREEM, AND ANDREW C. NOVICK

TABLE I. Demographics and overview of results

Patients (n)	12
Sex	
Male	7
Female	5
Mean age (yr)	68.5 ± 21
Mean follow-up (mo)	40.8 ± 32
Site (n)	
Upper pole	7
Inter-pole	3
Lower pole	2
T stage	
Tis	1
T1	3
T2	2
T3	6
Pathologic grade	
1	0
2	2
3	10
Negative surgical margins (n)	6
Tumor free (n)	4
Recurrence (n)	5 (42%)
Progression (n)	6 (50%)
Dialysis (n)	2
Death (n)	6 (follow-up 62 mo)
Urothelial cancer related	4
Patients with NED (n)	4
Alive (n)	6 (2 with metastasis)

KEY: NED = no evidence of disease.

Kidney autotransplantation after nephrectomy and work bench surgery as an ultimate approach to nephron-sparing surgery

Martin W. W. Janssen^{1*}, Johannes Linxweiler¹, Ines Philipps¹, Zentia Bütow^{1,2}, Stefan Siemer¹, Michael Stöckle¹ and Carsten-Henning Ohlmann¹

- 12 patients with solitary kidney
- 5 RCC, **5 UTUC**, 1 nephroblastoma, 1 met
- 3 required HD (25%)
 - 2 temp
 - 1 permanent
- NO UTUC recurrence

Laparoscopic Nephrectomy with Autotransplantation: Safety, Efficacy and Long-Term Durability

Geraldine Tran[#], Krishna Ramaswamy[#], Thomas Chi[†], Maxwell Meng, Christopher Freise, and Marshall L. Stoller

School of Medicine (GT), Department of Urology (KR, TC, MM, MLS) and Department of Surgery (CF), University of California, San Francisco, San Francisco, California

- 1/52 were for UTUC (CIS)
- +ve recurrence, with graft loss

Partial nephrectomy and autotransplantation with pyelovesicostomy for renal urothelial carcinoma in solitary kidneys: a clinical update

Joachim Steffens, Ulrich Humke*, Schahnaz Alloussi†, Manfred Zieglert† and Stefan Siemert†

*Departments of Urology and Paediatric Urology, St. Antonius Hospital Eschweiler, *Katharinenhospital Stuttgart and †University of Saarland, Hombérg/Saar Germany*

Accepted for publication 17 November 2006

- 4 patients
 - T1LG for all (two G2, two G1)
- none required HD
- all received adjuvant BCG/MMC
- no recurrences (mean f/u >6yrs)

ex-vivo NSS + Auto-Tx for UTUC

- Indications

- Solitary kidney/CKD pt

AND

- large renal pelvic/UPJ lesion
- large lesion filling single calyceal region
- long, multifocal ureteral lesion(s)

*** UTUC not amenable to endoscopic management, not amenable to ureteral reconstruction ***

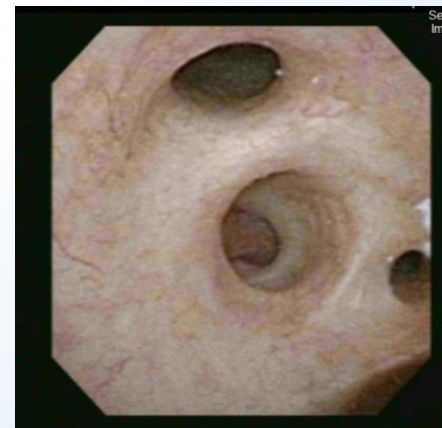
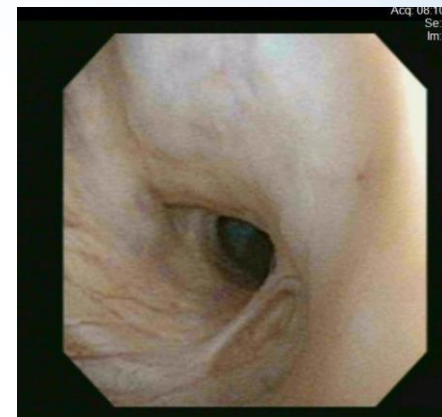
ex-vivo NSS + Auto-Tx for UTUC

- **Contraindications**

- high stage/grade lesion*
- lesions in multiple calyceal regions
- progressively declining renal function with ++ renal risk factors
- anatomic considerations (eg R kidney with short RV, ≥ 3 arteries, pelvic vascular calcifications, etc)

Technical Considerations for UTUC

- maximal ureteral cuff dissection, early cold perfusion
- ureteric lesions
 - excise entire ureter
 - pyelovesical anastomosis
 - frozen section for UPJ/RP tumours
- renal lesions
 - map out entire collecting system
 - consider intra-op renoscopy
 - can test for leaks
 - pyelovesical anastomosis

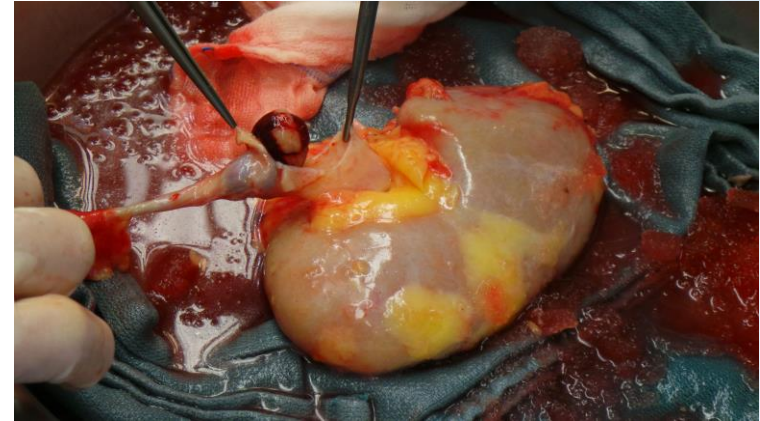


ex-vivo NSS + Auto-Tx for UTUC

- oncologic outcomes unknown
→ renal \neq ureteric
- improved ability to prevent need to RRT
- increased morbidity of other NSS options
- improved surveillance, adjuvant topical Rx

Auto-Tx in solitary kidney

- 7 cases
 - ureteral stricture 3
 - RCC 1
 - UTUC 2
 - Loin-pain hematuria 1
- 2 patients (29%) required temp HD, both had CKD



Auto-Tx for UTUC in solitary kidney

- UPJ T1LG } bladder recurrences only, no HD req'd, f/u 8yrs
- RP T1LG } no recurrences, temp HD post-op, f/u 3.5yrs
- LP T2HG } NAC, bladder recurrences only, no HD req'd but CKD3 now, f/u ~5yrs
- UPJ T1HG } local renal recurrence 6/12, req'd graft Nx, mets 6/12 later

Balancing Risks

- oncologic outcomes differ .. RCC >> UTUC
- up to 15-20% annual risk of mortality on HD
- avg life expectancy on HD is ~7yrs
 - 13-15yrs if in 40s
 - 2-4yrs for >65yrs
- transplant eligibility, wait times

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