MANAGEMENT OF SMALL RENAL MASSES

Prof. Alessandro VOLPE

University of Eastern Piedmont

Maggiore della Carità Hospital, Novara, Italy

BAU2018
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BELGIAN ASSOCIATION OF UROLOGY
Dolce – La Hulpe/Terhulpen 7 & 8 DECEMBER 2018

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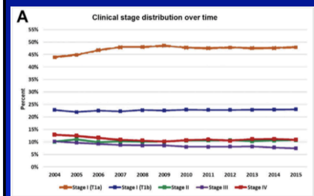
Clinical Stage Migration and Survival for Renal Cell Carcinoma in the United States

*Hiten D. Patel *, Mohit Gupta, Gregory A. Joice, Arnav Srivastava, Ridwan Alam, Mohamad E. Allaf, Phillip M. Pierorazio*

James Buchanan Brady Urological Institute and Department of Urology, Johns Hopkins University School of Medicine, Baltimore, MD, USA



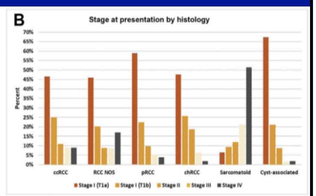


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Table 1 – Change in tumor size at presentation for renal cell carcinoma from 2004 to 2015 (National Cancer Database, 2004–2015).

	2004		2015			
Clinical stage	Median (mean), cm	IQR, cm	Median (mean), cm	IQR, cm	Coefficient, mm/yr[a]	*p* value
Stage I (T1a)	2.70 (2.75)	2.0–3.5	2.60 (2.67)	2.0–3.3	–0.079	<0.001
Stage I (T1b)	5.10 (5.52)	4.5–6.0	5.00 (5.18)	4.5–6.0	–0.262	<0.001
Stage I (All)	3.50 (3.70)	2.5–4.6	3.20 (3.48)	2.3–4.5	–0.144	<0.001
Stage II	9.00 (10.91)	8.0–11.0	8.90 (9.67)	7.6–10.6	–0.760	<0.001
Stage III	7.50 (8.30)	5.0–10.0	7.50 (8.22)	5.3–10.0	–0.026	0.851
Stage IV	8.00 (9.05)	5.6–11.0	8.20 (9.10)	5.8–11.0	0.140	0.299

Guidelines on Renal Cell Carcinoma

B. Ljungberg (chair), K. Bensalah, A. Bex (vice-chair), S. Canfield, S. Dabestani, F. Hofmann, M. Hora, M.A. Kuczyk, T. Lam, L. Marconi, A.S. Merseburger, P.F.A. Mulders, T. Powles, M. Staehler, A. Volpe

Recommendations	grade	
Offer surgery to achieve cure in localised renal cell cancer.	strong	↑↑
Offer partial nephrectomy to patients with T1 tumours.	strong	↑↑

Guideline for Management of the Clinical T1 Renal Mass

Steven C. Campbell,*,† Andrew C. Novick,‡ Arie Belldegrun,§ Michael L. Blute, George K. Chow, Ithaar H. Derwee... Raymond J. Leveillee,‖ Surena F. M...

From the American Urological Association Education and R...

- RN, particularly laparoscopic RN, is very appealing to patients and physicians but it is greatly overutilized.[9] Nephron-sparing approaches should be considered in all patients with a clinical T1 renal mass as an overriding principle, presuming adequate oncologic control can be achieved, based on

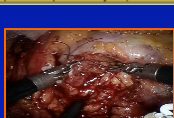
NCCN Clinical Practice Guidelines in Oncol...

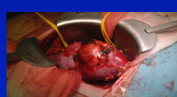
Kidney Cancer

- Nephron-sparing surgery (partial nephrectomy) is appropriate in selected patients, for example:
  - Small unilateral tumors (T1a and selected patients T1b)
  - Uninephric state, renal insufficiency, bilateral renal masses, familial renal cell cancer

EAU Guidelines on Renal Cell Carcinoma

Recommendations	Strength rating
Offer surgery to achieve cure in localised renal cell cancer.	Strong
Offer partial nephrectomy to patients with T1 tumours.	Strong



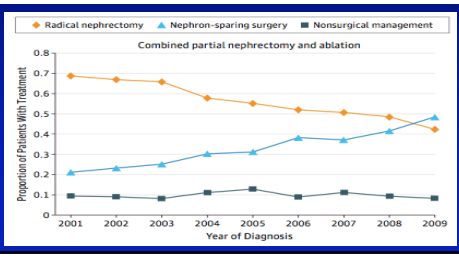


Original Investigation

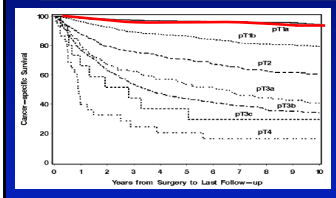
Management of Small Kidney Cancers in the New Millennium
Contemporary Trends and Outcomes in a Population-Based Cohort

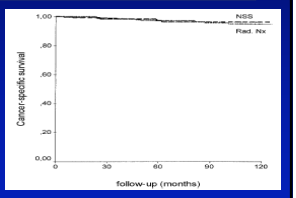
JAMA Surg. doi:10.1001/jamasurg.2015.0294
Published online May 27, 2015.

William C. Huang, MD; Coral L. Atoria, MPH; Marc Bjurlin, MsC, DO; Laura C. Pinheiro, MPH; Paul Russo, MD; William T. Lowrance, MD, MPH; Elena B. Elkin, PhD



pT1a RCC SURGICAL OUTCOMES





Frank et al, J Urol 2005

Patard et al, J Urol 2004

A Prospective, Randomised EORTC Intergroup Phase 3 Study Comparing the Oncologic Outcome of Elective Nephron-Sparing Surgery and Radical Nephrectomy for Low-Stage Renal Cell Carcinoma

Hendrik Van Poppel [a,], Luigi Da Pozzo [b,1], Walter Albrecht [c], Vsevolod Matveev [d], Aldo Bono [e], Andrzej Borkowski [f], Marc Colombel [g], Laurence Klotz [h], Eila Skinner [i], Thomas Keane [j], Sandrine Marreaud [k], Sandra Collette [k], Richard Sylvester [k]*

There were 12 renal cancer–related deaths: 4 in the RN group and 8 in the NSS group. The estimated risk of death from renal cancer was not significantly higher in the NSS arm (HR: 2.06), with a very wide CI (95% CI, 0.62–6.81; Gray's test $p = 0.23$) resulting from the small number of renal cancer–related deaths.

Conclusions	LE
Partial nephrectomy achieves similar oncological outcomes of radical nephrectomy for clinically localized renal tumours (cT1).	1b

Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study

William C Huang, Andrew S Levey, Angel M Serio, Mark Snyder, Andrew J Vickers, Ganesh V Raj, Peter T Scardino, Paul Russo

http://oncology.thelancet.com Vol 7 September 2006

eGFR <60 ml/min

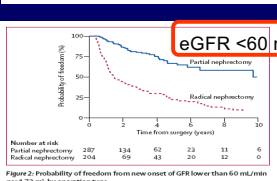


Figure 2: Probability of freedom from new onset of GFR lower than 60 mL/min per 1.72 m², by operation type

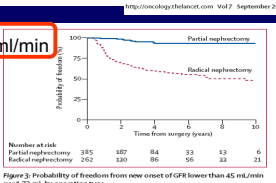


Figure 3: Probability of freedom from new onset of GFR lower than 45 mL/min per 1.72 m², by operation type

Interpretation Because the baseline kidney function of patients with renal cortical tumours is lower than previously thought, accurate assessment of kidney function is essential before surgery. Radical nephrectomy is a significant risk factor for the development of chronic kidney disease and might no longer be regarded as the gold standard treatment for small, renal cortical tumours.

Renal Function After Nephron-sparing Surgery Versus Radical Nephrectomy: Results from EORTC Randomized Trial 30904

Emil Scosyrev [a], Edward M. Messing [a,], Richard Sylvester [b], Steven Campbell [c], Hendrik Van Poppel [d]*

[a] Department of Urology, University of Rochester Medical Center, Rochester, NY, USA; [b] Department of Biostatistics, EORTC Headquarters, Brussels, Belgium; [c] Department of Urology, Cleveland Clinic, Cleveland, OH, USA; [d] Department of Urology, University Hospital K.U. Leuven, Leuven, Belgium

Table 2 – Analysis of lowest estimated glomerular filtration rate (eGFR) and last eGFR according to specified binary cut-offs, by assigned treatment (median follow-up 6.7 yr)

		RN (n = 259)		NSS (n = 255)				
eGFR	Outcome	No.	%	No.	%	Difference, %	95% CI	p*
Lowest	eGFR <60	222	85.7	165	64.7	21.0	(13.8–28.3)	<0.001
	eGFR <30	26	10.0	16	6.3	3.7	(−1.0 to 8.5)	
	eGFR <15	4	1.5	4	1.6	−0.1	(−2.2 to 2.1)	
Last	eGFR <60	152	58.7	98	38.4	20.3	(11.9–28.7)	<0.001
	eGFR <45	64	24.7	34	13.3	11.4	(4.7–18.1)	
	eGFR <30	17	6.6	9	3.5	3.1	(−0.7 to 6.8)	
	eGFR <15	3	1.2	2	0.8	0.4	(−1.3 to 2.1)	

CI = confidence interval; NSS = nephron-sparing surgery; RN = radical nephrectomy.
* Wilcoxon-Mann-Whitney test.

Renal Function After Nephron-sparing Surgery Versus Radical Nephrectomy: Results from EORTC Randomized Trial 30904

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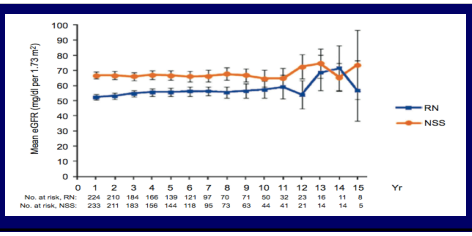
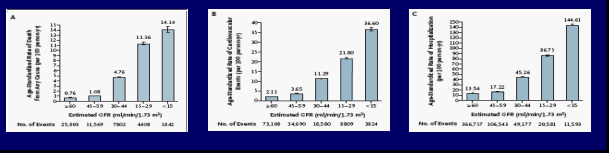


The NEW ENGLAND JOURNAL of MEDICINE

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.



Radical Nephrectomy for pT1a Renal Masses May be Associated With Decreased Overall Survival Compared With Partial Nephrectomy

R. Houston Thompson,* Stephen A. Boorjian, Christine M. Lohse, Bradley C. Leibovich, Eugene D. Kwon, John C. Cheville and Michael L. Blute

From the Departments of Urology (RHT, SAB, BCL, EDK, MLB), Health Sciences Research (CML) and Laboratory Medicine and Pathology (JCC), Mayo Medical School and Mayo Clinic, Rochester, Minnesota

Partial Nephrectomy Versus Radical Nephrectomy in Patients With Small Renal Tumors—Is There a Difference in Mortality and Cardiovascular Outcomes?

William C. Huang,* Elena B. Elkin, Andrew S. Levey, Thomas L. Jang and Paul Russo

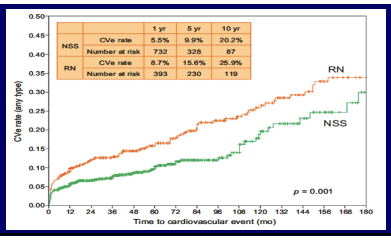
Partial Nephrectomy Is Associated with Improved Overall Survival Compared to Radical Nephrectomy in Patients with Unanticipated Benign Renal Tumours

*Christopher J. Weight, Gregory Lieser, Benjamin T. Larson, Tianming Gao, Brian R. Lane, Steven C. Campbell, Inderbir S. Gill, Andrew C. Novick, Amr F. Fergany **

Glickman Urologic and Kidney Institute, Cleveland Clinic, Cleveland, Ohio, USA

Nephron-sparing Techniques Independently Decrease the Risk of Cardiovascular Events Relative to Radical Nephrectomy in Patients with a T1a–T1b Renal Mass and Normal Preoperative Renal Function

Umberto Capitanio [a,b,], Carlo Terrone [c], Alessandro Antonelli [d], Andrea Minervini [e], Alessandro Volpe [c], Maria Furlan [d], Rayan Matloob [a,b], Federica Regis [c], Cristian Fiori [f], Francesco Porpiglia [f], Ettore Di Trapani [a,b], Monica Zacchero [c], Sergio Serni [e], Andrea Salonia [a,b], Marco Carini [e], Claudio Simeone [d], Francesco Montorsi [a,b], Roberto Bertini [a,b]*



A Prospective, Randomised EORTC Intergroup Phase 3 Study Comparing the Oncologic Outcome of Elective Nephron-Sparing Surgery and Radical Nephrectomy for Low-Stage Renal Cell Carcinoma

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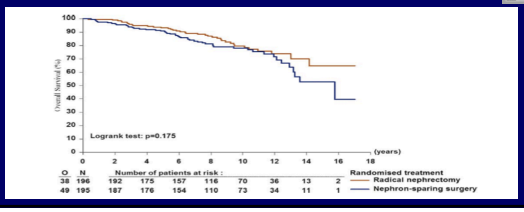
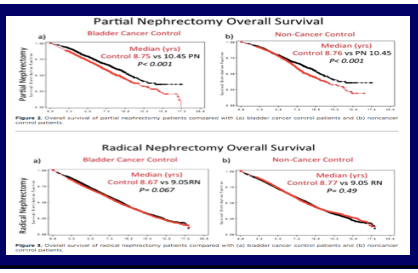


Original Article

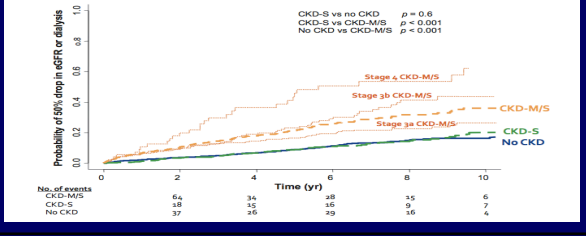
Overall Survival Advantage with Partial Nephrectomy: A Bias of Observational Data?

Brian Shuch, MD[1,2]; Janet Hanley, MS[3]; Julie Lai, MPH[3]; Srinivas Vourganti, MD[2]; Simon P. Kim, MD, MPH[1,4]; Claude M. Setodji, PhD[3]; Andrew W. Dick, PhD[3]; Wong-Ho Chow, PhD[3]; and Chris Saigal, MD, MPH[4]; and the Urologic Diseases in America Project



Survival and Functional Stability in Chronic Kidney Disease Due to Surgical Removal of Nephrons: Importance of the New Baseline Glomerular Filtration Rate

Brian R. Lane [a], Sevag Demirjian [b], Ithaar H. Derweesh [c], Toshio Takagi [b], Zhiling Zhang [b,d], Lily Velet [b], Cesar E. Ercole [b], Amr F. Fergany [b], Steven C. Campbell [b,]*



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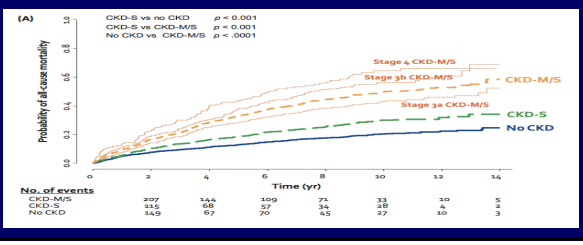
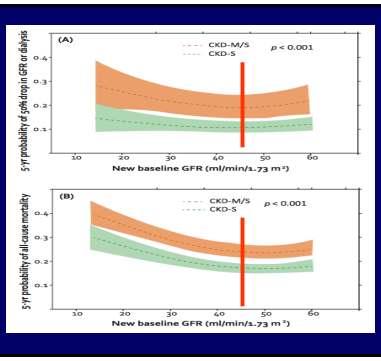
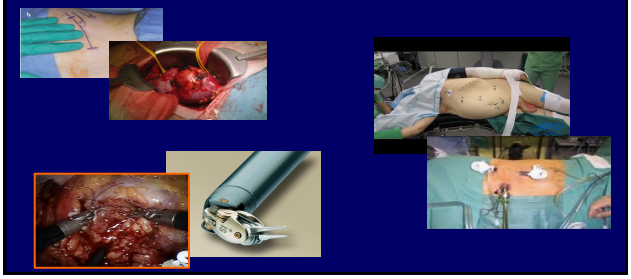




NEPHRON SPARING SURGERY
Minimally invasive evolution



Comparison of Perioperative Outcomes Between Robotic and Laparoscopic Partial Nephrectomy: A Systematic Review and Meta-analysis

Ji Eun Choi [a], Ji Hye You [a], Dae Keun Kim [b], Koon Ho Rha [b,], Seon Heui Lee [c,*]*

Studies included in meta-analysis (*n* = 23)

2240 RAPN

No significant difference in:
- operative time
- estimated blood loss
- complication rate
- positive margins

Lower rate of conversion to open /radical surgery (p=0.02)

Shorter length of stay (p=0.04)

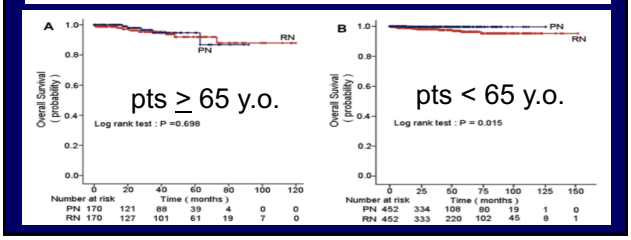
Shorter WIT (p=0.005) and smaller eGFR change (p=0.03)

EAU Guidelines on Renal Cell Carcinoma

Partial nephrectomy can be performed, either with an open, pure laparoscopic or robot-assisted approach, based on surgeon's expertise and skills.	2b

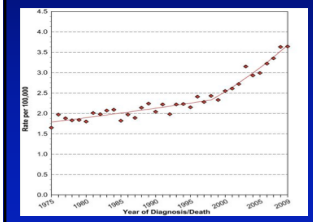
Overall survival and renal function after partial and radical nephrectomy among older patients with localised renal cell carcinoma: A propensity-matched multicentre study

Jae Seung Chung [a], Nak Hoon Son [b], Sang Eun Lee [c], Sung Kyu Hong [c], Sang Chul Lee [c], Cheol Kwak [d], Sung Hoo Hong [e], Yong June Kim [f], Seok Ho Kang [g], Seok-Soo Byun [c,*]

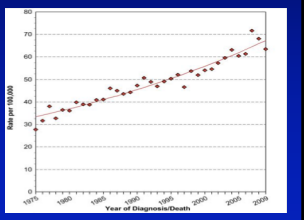


National Cancer Institute

Surveillance Epidemiology and End Results



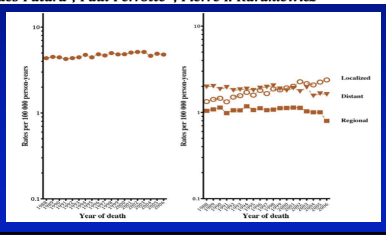
< 50 years



> 75 years

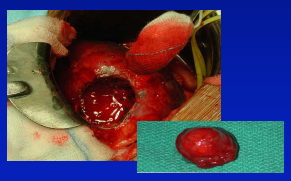
Age-Adjusted Incidence, Mortality, and Survival Rates of Stage-Specific Renal Cell Carcinoma in North America: A Trend Analysis

Maxine Sun [a,,1], Rodolphe Thuret [a,b,1], Firas Abdollah [a,c], Giovanni Lughezzani [a,c], Jan Schmitges [d], Zhe Tian [a], Shahrokh F. Shariat [e], Francesco Montorsi [c], Jean-Jacques Patard [f], Paul Perrotte [g], Pierre I. Karakiewicz [a,g]*



SMALL RENAL MASSES NATURAL HISTORY

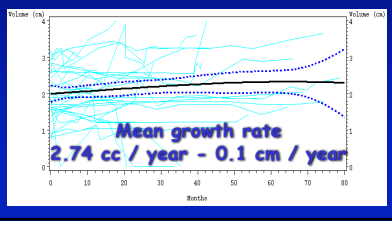
Natural history of renal tumors has been poorly understood since the gold standard treatment is surgical removal soon after diagnosis



The Natural History of Incidentally Detected Small Renal Masses

Alessandro Volpe, M.D.[1]
Tony Panzarella, M.Sc.[2]
Ricardo A. Rendon, M.D.[3]
Masoom A. Haider, M.D.[4]
Filippos I. Kondylis, M.D.[1]
Michael A. S. Jewett, M.D.[1]

BACKGROUND. The incidence of renal cell carcinoma (RCC) is increasing, largely due to the widespread use of cross-sectional imaging. Most renal tumors are detected incidentally as small, asymptomatic masses. To study their natural history, the authors prospectively followed a series of patients with this type of lesion who were unsuited for or refused surgery.
METHODS. Twenty-nine patients with 32 masses that measured < 4 cm in greatest dimension (25 solid masses and 7 complex cystic masses) were studied. The



Cancer, 2004

VIEWPOINT

NATURE CLINICAL PRACTICE UROLOGY XXX 2007 VOL 4 NO X

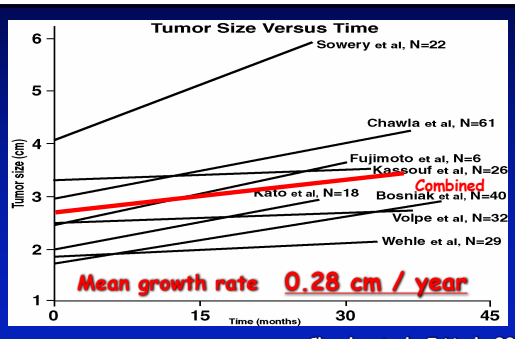
The role of surveillance for small renal masses

Alessandro Volpe and Michael AS Jewett*

ACTIVE SURVEILLANCE

Initial monitoring of growth rate and clinical behaviour of a SRM with serial abdominal imaging

Delayed treatment for tumors who show a fast growth or clinical progression during follow-up



Chawla et al, J Urol, 2006

Review Articles

The Natural History of Observed Enhancing Renal Masses: Meta-Analysis and Review of the World Literature

Sam N. Chawla, Paul L. Crispen, Alexandra L. Hanlon, Richard E. Greenberg, David Y. T. Chen and Robert G. Uzzo*
From the Departments of Urologic Oncology and Biostatistics (ALH), Fox Chase Cancer Center, Temple University School of Medicine, Philadelphia, Pennsylvania

Purpose: Standard therapy for an enhancing renal mass is surgical. However, operative treatment may not be plausible in all clinical circumstances. Data on the natural history of untreated enhancing renal lesions is limited but could serve as a decision making resource for patients and physicians. We examined available data on the natural history of observed solid renal masses.

TABLE 2. *Meta-Analysis of available pathological findings in renal masses that underwent observation*

References	No. Lesions	No. Pathological Findings Available (%)	No. RCC Pos (%)	No. Benign (%)	No. Progression to M+ (%)
Fujimoto et al[21]	6	6 (100)	6 (100)	0	0
Bosniak et al[12,13]	40	28 (65)	22 (85)	4 (15)	0
Oda et al[14]	16	16 (100)	16 (100)	0	0
Kassouf et al[16]	26	4 (15)	4 (100)	0	0
Volpe et al[17]	32	9 (28)	8 (89)	1 (11)	0
Wehle et al[18]	29	5 (17)	4 (80)	1 (20)	0
Kato et al[15]	18	18 (100)	18 (100)	0	0
Lamb et al[19]	36	24 (67)	23 (96)	1 (4)	1 (3)
Sowery and Siemens[20]	22	2 (9)	2 (100)	0	1 (5)
Present series	81	31 (34)	17 (81)	4 (19)	1 (2)
Totals	286	131 (46)	120 (92)	11 (8)	3 (1)

Small Renal Masses Progressing to Metastases Under Active Surveillance

A Systematic Review and Pooled Analysis

Cancer February 15, 2012

Marc C. Smaldone, MD[1]; Alexander Kutikov, MD[1]; Brian L. Egleston, MPP, PhD[2]; Daniel J. Canter, MD[1]; Rosalia Viterbo, MD[1]; David Y. T. Chen, MD[1]; Michael A. Jewett, MD[3]; Richard E. Greenberg, MD[1]; and Robert G. Uzzo, MD[1]

18 studies

880 patients - 936 renal masses

18 progressions to mets (2%)

after a mean follow-up of 40.2 months

Mean linear growth rate: 0.31 cm/year

Mean volume growth rate: 6.3 cm^3/year

Active Surveillance of Small Renal Masses: Progression Patterns of Early Stage Kidney Cancer

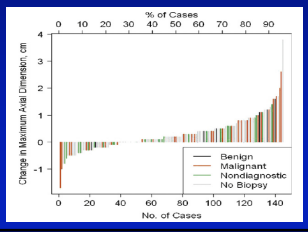
Michael A.S. Jewett[a,], Kamal Mattar[a], Joan Basiuk[a], Christopher G. Morash[b], Stephen E. Pautler[c], D. Robert Siemens[d], Simon Tanguay[e], Ricardo A. Rendon[f], Martin E. Gleave[g], Darrel E. Drachenberg[h], Raymond Chow[i], Hannah Chung[a], Joseph L. Chin[j], Neil E. Fleshner[a], Andrew J. Evans[k], Brenda L. Gallie[l], Masoom A. Haider[m], John R. Kachura[m], Ghada Kurban[n], Kimberly Fernandes[n], Antonio Finelli[a]*

209 incidental SRMs (<4 cm)

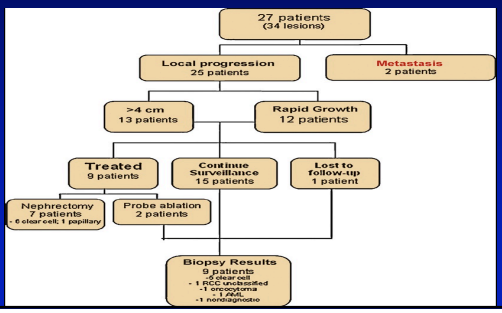
Mean size 2.1 cm (0.4-4)

Mean follow-up 28 mo (1-60)

Mean growth rate 0.13 cm/year



Active Surveillance of Small Renal Masses: Progression Patterns of Early Stage Kidney Cancer



Active Surveillance for Localized Renal Masses: Tumor Growth, Delayed Intervention Rates, and >5-yr Clinical Outcomes

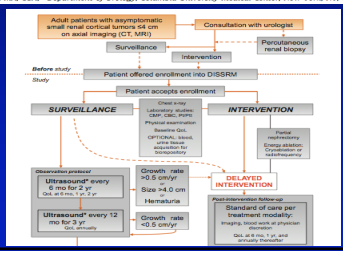
Andrew G. McIntosh[a,b,], Benjamin T. Ristau[b,c], Karen Ruth[b], Rachel Jennings[d], Eric Ross[b], Marc C. Smaldone[b], David Y.T. Chen[b], Rosalia Viterbo[b], Richard E. Greenberg[b], Alexander Kutikov[b], Robert G. Uzzo[b]*

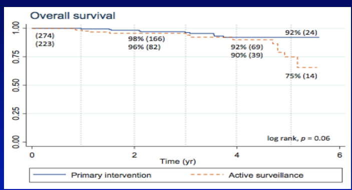
Results and limitations: Median follow-up was 67 mo (interquartile range [IQR] 41–94 mo) for surviving patients. Cumulative incidence of DI (n = 153) after 1, 2, 3, 4, and 5 yr was 9%, 22%, 29%, 35%, and 42%, respectively. Median initial maximum tumor dimension was 2.1 cm (IQR 1.5–3.1 cm). Median iLGR and overall LGR were 1.9 (IQR 0–7) and 1.9 (IQR 0.3–4.2) mm/yr, respectively. Compared with the no growth group, low iLGR (hazard ratio [HR] 1.25, 95% cumulative incidence [CI] 0.82–1.91), moderate iLGR (HR 2.1, 95% CI 1.31–3.36), and high iLGR (HR 1.87, 95% CI 1.23–2.84) were associated with DI (p = 0.003). The iLGR was not associated with OS (p = 0.8). DI was not associated with OS (HR 1.34, 95% CI 0.79–2.29, p = 0.3). Five-year cancer-specific mortality (CSM) was 1.2% (95% CI 0.4–2.8%). Of 99 patients on AS without DI for >5 yr, one patient metastasized.

Conclusions: At >5 yr, AS ± DI is a successful strategy in carefully managed patients. DI often occurs in the first 2–3 yr, becoming less likely over time. Rare metastasis and low CSM rates should reassure physicians that AS is safe in the intermediate to long term.

Five-year Analysis of a Multi-institutional Prospective Clinical Trial of Delayed Intervention and Surveillance for Small Renal Masses: The DISSRM Registry

Phillip M. Pierorazio[a,], Michael H. Johnson[a], Mark W. Ball[a], Michael A. Gorin[a], Bruce J. Trock[a], Peter Chang[b], Andrew A. Wagner[b], James M. McKiernan[c], Mohamad E. Allaf[a]*
[a] The James Buchanan Brady Urological Institute and Department of Urology, Johns Hopkins Medicine, Baltimore, MD, USA; [b] Division of Urology, Beth Israel Deaconess Medical Center, Boston, MA, USA; [c] Department of Urology, Columbia University Medical Center, New York, NY, USA





lesions. OS for PI and AS was 98% and 96% at 2 yr, and 92% and 75% at 5 yr, respectively (log rank, $p = 0.06$). At 5 yr, CSS was 99% and 100% for PI and AS, respectively ($p = 0.3$). AS was not predictive of OS or CSS in regression modeling with relatively short follow-up. ***Conclusions:*** In a well-selected cohort with up to 5 yr of prospective follow-up, AS was not inferior to PI.

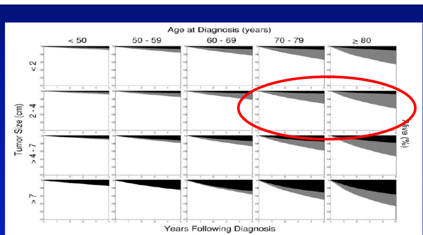
WHITMORE APHORISM

Is it possible to cure **renal cancer** when it is necessary and is it necessary to cure **renal cancer** when it is possible?

Five-Year Survival After Surgical Treatment for Kidney Cancer

A Population-Based Competing Risk Analysis

John M. Hollingsworth, MD[1]
David C. Miller, MD, MPH[2]
Stephanie Daignault, MS[1]
Brent K. Hollenbeck, MD, MS[1]



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DOI 10.1002/cncr.22600
Published online 9 March 2007 in Wiley InterScience (www.interscience.wiley.com).

Active Treatment of Localized Renal Tumors May Not Impact Overall Survival in Patients Aged 75 Years or Older

Cancer July 1, 2010

Brian R. Lane, MD, PhD[1]; Robert Abouassaly, MD[1]; Tianming Gao, MS[2]; Christopher J. Weight, MD[1]; Adrian V. Hernandez, MD, PhD[2]; Benjamin T. Larson, MD[1]; Jihad H. Kaouk, MD[1]; Inderbir S. Gill, MD[1]; and Steven C. Campbell, MD, PhD[1]

537 clinical T1 renal tumors

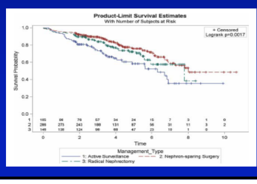


Table 2. Cox Proportional Hazards Model of All-Cause Mortality

Variable	Univariate Analysis HR (95% CI)	P	Multivariate Analysis HR (95% CI)	P
Management type		.0021		.22[a]
Radical nephrectomy	0.64 (0.42-0.99)		0.75 (0.45-1.26)	
Nephron-sparing intervention	0.50 (0.34-0.73)		0.67 (0.42-1.05)	
Active surveillance	1.00		1.00	
Age, per 5-y increase	1.36 (1.16-1.60)	.0002	1.34 (1.11-1.60)	.002
Men	0.94 (0.67-1.30)	.69	0.86 (0.61-1.22)	.40
Race		.25		.64
Caucasian	1.99 (0.63-6.24)		1.65 (0.52-5.26)	
African American	2.68 (0.78-9.22)		1.83 (0.52-6.50)	
Other	1.00		1.00	
Charlson comorbidity index, per 1-unit increase	1.35 (1.23-1.48)	<.0001	1.33 (1.20-1.48)	<.0001
Clinical size, per 1-cm increase	1.13 (1.02-1.25)	.02	1.09 (0.97-1.22)	.16
Solitary kidney	1.10 (0.70-1.76)	.68	1.16 (0.69-1.93)	.58
Bilateral renal involvement	0.86 (0.49-1.52)	.61	1.12 (0.61-2.04)	.72
Initial GFR, per 10 mL/min/1.73m² decrease	1.11 (1.03-1.20)	.0079	1.02 (0.93-1.11)	.68

HR indicates hazard ratio; CI, confidence interval; GFR, glomerular filtration rate.
[a] P values for multivariate pair-wise comparisons: radical nephrectomy versus surveillance, $P = .28$; nephron-sparing intervention versus surveillance, $P = .08$.

BJUI

Active surveillance of small renal masses offers short-term oncological efficacy equivalent to radical and partial nephrectomy

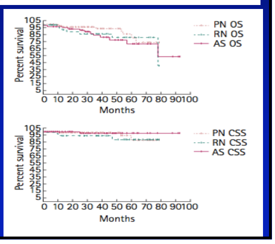
Nilay Patel, David Cranston, M. Zeeshan Akhtar, Caroline George, Andrew Jones, Aaron Leiblich, Andrew Protheroe and Mark Sullivan
Department of Urology, Churchill Hospital, Headington, Oxford, UK

234 T1a renal masses

- 71 surveillance
- 41 radical nephrectomy
- 90 partial nephrectomy

Mean follow-up of 34 months

No significant difference in OS and CSS between groups



Management of Localized Kidney Cancer: Calculating Cancer-specific Mortality and Competing Risks of Death for Surgery and Nonsurgical Management

Maxine Sun[a,b,1,], Andreas Becker[a,c,1], Zhe Tian[a], Florian Roghmann[a,d], Firas Abdollah[a,e], Alexandre Larouche[a], Pierre I. Karakiewicz[a,f], Quoc-Dien Trinh[a,f]*

[a] Cancer Prognostics and Health Outcomes Unit, University of Montreal Health Center, Montreal, Canada; [b] Department of Public Health, Faculty of Medicine, University of Montreal, Montreal, Canada; [c] Martini-Clinic, Prostate Cancer Center Hamburg-Eppendorf, Hamburg, Germany; [d] Department of Urology, Universitätsklinik Marienhospital, Herne, Germany; [e] Department of Urology, Vita-Salute San Raffaele University, Milan, Italy; [f] Department of Urology, University of Montreal Health Center, Montreal, Canada

	PN vs NSM, HR (CI)	p value	RN vs NSM, HR (CI)	p value
Cancer-specific mortality				
Primary analyses				
Entire cohort, n = 10 595	0.45 (0.24–0.83)	0.01	0.58 (0.35–0.96)	0.03
T1a, n = 6443	0.41 (0.18–0.91)	0.03	0.47 (0.23–0.98)	0.04
Subanalyses				
≥75 yr, n = 4830	0.48 (0.20–1.14)	0.1	0.57 (0.32–1.03)	0.1
T1a and ≥75 yr, n = 2873	0.39 (0.13–1.08)	0.1	0.40 (0.16–1.01)	0.1
Other-cause mortality				
Primary analyses				
Entire cohort, n = 10 595	0.51 (0.37–0.69)	<0.001	0.59 (0.45–0.79)	0.03
T1a, n = 6443	0.48 (0.32–0.70)	<0.001	0.61 (0.43–0.87)	0.006
Subanalyses				
≥75 yr, n = 4830	0.55 (0.36–0.83)	0.004	0.61 (0.42–0.89)	0.01
T1a and ≥75 yr, n = 2873	0.47 (0.28–0.77)	0.003	0.56 (0.35–0.89)	0.02

Guidelines on Renal Cell Carcinoma

Recommendation	grade	
Offer active surveillance, radiofrequency ablation and cryoablation to elderly and/or comorbid patients with small renal masses.	weak	↑

Guideline for Management of the Clinical T1 Renal Mass

Steven C. Campbell,*,† Andrew C. Novick,‡ Arie Belldegrun,§ Michael L. Blute, George K. Chow, Ithaar H. Derweesh, Martha M. Faraday, Jihad H. Kaouk,¶ Raymond J. Leveillee,‖ Surena F. Matin,** Paul Russo†† and Robert G. Uzzo‡‡

From the American Urological Association Education and Research, Inc., Linthicum, Maryland

- Active surveillance is a reasonable option for the management of localized renal masses that should be discussed with all patients and should be a primary consideration for patients with decreased life expectancy or extensive comorbidities that would make them high risk for intervention[30,39] For patients who are

NCCN Clinical Practice Guidelines in Oncology™

Kidney Cancer

Patients in satisfactory medical condition should undergo surgical excision of stage I through III tumors. However, a small set of elderly or infirm patients with small tumors may be offered surveillance alone or energy ablative techniques, such as radiofrequency ablation or cryoablation (KID-A)

ACTIVE SURVEILLANCE OF SRMs
Limitations of clinical evidence

Short-intermediate term follow-up outcomes

Lack of standardized criteria to indicate delayed intervention

Limited information on patient's QoL and anxiety

Lack of pathological diagnosis in most cases

European Active SurveillancE of Renal Cell Carcinoma

EASE

EASE STUDY

eau rf Research Foundation

Multicentre prospective study of active surveillance of small, histologically confirmed RCCs

Standardized indications, follow-up, criteria for progression and to indicate delayed intervention

European Active SurveillancE of Renal Cell Carcinoma

EASE

EASE STUDY

eau rf Research Foundation

PRIMARY OBJECTIVE

To assess overall survival of patients

with incidental, histologically biopsy-confirmed

<4 cm renal cell carcinomas

managed conservatively with active surveillance

SECONDARY OBJECTIVES

- To demonstrate that OS is not significantly different compared to OS of the general population with similar age and co-morbidities and without RCC
- To assess growth and progression rate of small RCCs
- To assess cancer-specific and progression-free survival of patients with small RCCs in AS
- To identify genetic and molecular biomarkers of fast tumor progression and metastases

INCLUSION CRITERIA

- Males or females, age ≥ 18 years.
- Incidental diagnosis of a <4 cm solid renal mass
- Histologically confirmed RCC by percutaneous needle biopsy at diagnosis
- Patients unfit for active treatment due to advanced age, or co-morbidity or choosing to avoid active treatment
- Preparedness to comply with percutaneous tumor biopsy and a close follow-up protocol

STUDY CALENDAR

	Baseline	Mth 3	Mth 6	Mth 12	Mth 18	Mth 24	Mth 30	Mth 36	Yearly	TP[1]
Informed consent	X									
Demographics	X									
Medical History	X	X	X	X	X	X	X	X	X	X
Concurrent medications	X	X	X	X	X	X	X	X	X	X
Charlson Comorbidity Index	X		X	X		X		X	X	X
ECOG Performance status	X		X	X		X		X	X	X
EORTC QLQ-C30/ HADS	X		X	X		X		X	X	X
Physical exam	X	X	X	X	X	X	X	X	X	X
BMI (weight and length)	X		X	X		X		X	X	X
Serum creatinine/eGFR	X		X	X		X		X	X	X
Cell blood count	X		X	X		X		X	X	
Liver functions	X		X	X		X		X	X	X
Abdominal imaging	X	X	X	X	X	X	X	X	X	X
Chest imaging	X	X	X	X	X	X	X	X	X	X
Blood collection and storage	X		X	X		X		X	X	X
Urine Collection and storage[2]	X		X	X		X		X	X	X
Percutaneous needle biopsy	X									X[3]
Tumor tissue storage	X									X[3]
Pathological images upload	X									X[3]

TUMOR PROGRESSION

Patients will be followed until

- Tumor progression
  - tumor volume doubling time < 12 months
  - maximum tumor diameter > 4 cm
  - increase in TNM stage
  - unequivocal evidence of distant metastases
  - development of tumor related symptoms requiring surgical or other treatment

CENTRES INVOLVED

65 centres invited

ale.volpe@me.com

Italy, France, United Kingdom, The Netherlands, Spain, Portugal, Austria, Germany, Switzerland, Ireland, Sweden, Finland, Norway, Iceland, Argentina, Hong Kong

27 centres submitted protocol for ethics approval

17 centres obtained ethics approval

16 centres are actively recruiting

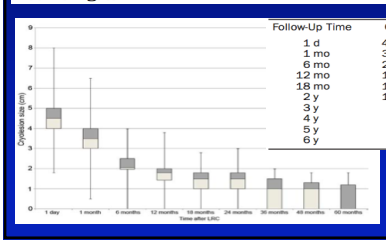
TARGET POPULATION: 400 patients

RCC
NON SURGICAL MANAGEMENT

- ABLATIVE THERAPY
  - PERCUTANEOUS or LAP-ASSISTED
  - *"freezing"* or *"heating"*
    - CRYOABLATION
    - RADIOFREQUENCY ABLATION (RFA)
    - MIRCROWAVE ABLATION, HIFU…

Oncologic Results of Laparoscopic Renal Cryoablation for Clinical T1a Tumors: 8 Years of Experience in a Single Institution

Giorgio Guazzoni, Andrea Cestari, Nicolòmaria Buffi, Giovanni Lughezzani, Luciano Nava, Gianpiero Cardone, Giuseppe Balconi, Massimo Lazzeri, Francesco Montorsi, and Patrizio Rigatti

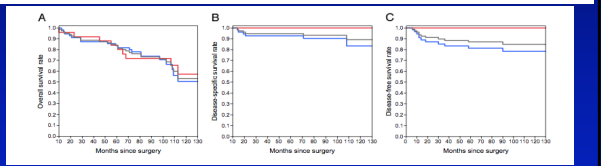


Follow-Up Time	Cryolesion (mm)	Reduction (%)
1 d	44.5 ± 9.4 (45)	—
1 mo	36.3 ± 9.4 (35)	18
6 mo	22.2 ± 8.01 (20)	27
12 mo	17.8 ± 7.5 (18)	43
18 mo	13.1 ± 7.0 (15)	60
2 y	13.1 ± 7.0 (14)	60
3 y	8.9 ± 7.0 (10)	73
4 y	8.1 ± 6.4 (10)	76
5 y	5.1 ± 6.8 (0)	83
6 y	4.0 ± 5.7 (0)	87

Laparoscopic Renal Cryoablation: 8-Year, Single Surgeon Outcomes

Monish Aron,* Kazumi Kamoi, Erick Remer, Andre Berger, Mihir Desai and Inderbir Gill

From the Departments of Urology and Radiology, Cleveland Clinic, Cleveland, Ohio (KK, ER), and Catherine and Joseph Aresty Department of Urology, University of Southern California Institute of Urology, Keck School of Medicine, University of Southern California, Los Angeles, California



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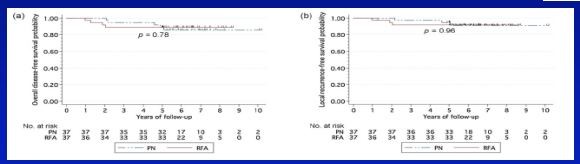
Radiofrequency Ablation Versus Partial Nephrectomy in Patients with Solitary Clinical T1a Renal Cell Carcinoma: Comparable Oncologic Outcomes at a Minimum of 5 Years of Follow-Up

Ephrem O. Olweny [a], Samuel K. Park [a], Yung K. Tan [a], Sara L. Best [a], Clayton Trimmer [b], Jeffrey A. Cadeddu [a,]*



91.8% ($p = 0.35$), respectively. Study limitations are retrospective data analysis, loss to follow-up, limited statistical power, and limited generalizability of our data.

Laparoscopic Cryoablation Versus Partial Nephrectomy for the Treatment of Small Renal Masses: Systematic Review and Cumulative Analysis of Observational Studies

Tobias Klatte [a,], Bernhard Grubmüller [a], Matthias Waldert [a], Peter Weibl [a], Mesut Remzi [b]*

[a] Department of Urology, Medical University of Vienna, Vienna, Austria
[b] Department of Urology, Landesklinikum Weinviertel, Korneuburg, Austria

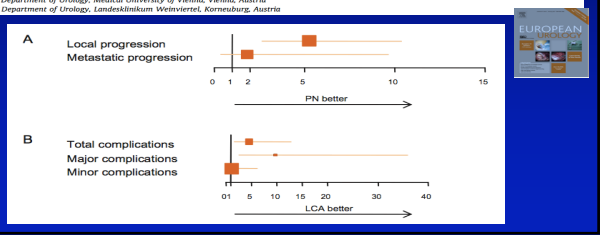
	Local progression			Metastatic progression		
Covariate	RR	95% CI	p	RR	95% CI	p
LCA vs PN	5.24	2.67–10.28	<0.001	1.86	0.36–9.65	0.465
Mean age	0.98	0.93–1.03	0.443	0.98	0.84–1.13	0.779
Mean size	1.85	1.23–2.78	0.003	1.02	0.38–2.70	0.970
Mean follow-up	0.99	0.98–1.00	0.200	1.00	0.98–1.02	0.272

RR = risk ratio; CI = confidence interval; LCA = laparoscopic cryoablation; PN = partial nephrectomy.
* LCA and greater tumor sizes were independent adverse predictors of local progression. RRs with 95% CIs are presented.

Laparoscopic Cryoablation Versus Partial Nephrectomy for the Treatment of Small Renal Masses: Systematic Review and Cumulative Analysis of Observational Studies

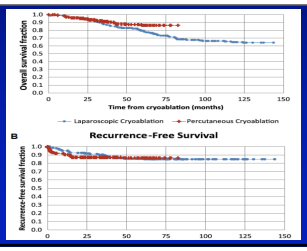
Tobias Klatte [a,], Bernhard Grubmüller [a], Matthias Waldert [a], Peter Weibl [a], Mesut Remzi [b]*

[a] Department of Urology, Medical University of Vienna, Vienna, Austria
[b] Department of Urology, Landesklinikum Weinviertel, Korneuburg, Austria



Comparison of Laparoscopic and Percutaneous Cryoablation for Treatment of Renal Masses

Eric H. Kim, Youssef S. Tanagho, Nael E. Saad, Sam B. Bhayani, and R. Sherburne Figenshau



Comparison of Laparoscopic and Percutaneous Cryoablation for Treatment of Renal Masses

Eric H. Kim, Youssef S. Tanagho, Nael E. Saad, Sam B. Bhayani, and R. Sherburne Figenshau

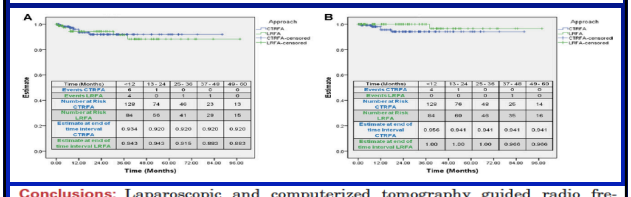
Mean length of stay was shorter for patients undergoing PCA as compared with LCA. Complication rates and decline in renal function at most recent follow-up were similar between groups. Oncologic outcomes were influenced by baseline patient and tumor characteristics rather than the cryoablation approach. UROLOGY 83: 1081–1087, 2014. © 2014 Elsevier Inc.

	Overall Survival			Recurrence-free Survival		
Variable	HR	95% CI	P	HR	95% CI	P
LCA vs PCA	1.42	0.68-2.97	.36	1.11	0.45-2.73	.82
Tumor size ≥3 cm	1.58	0.91-2.72	.10	**2.85**	**1.33-6.10**	**<.01**
Age-adjusted CCI ≥6	**2.17**	**1.18-4.00**	**.01**	0.57	0.29-1.14	.11
BMI ≥ 30 kg/m^2	1.05	0.63-1.76	.84	**2.35**	**1.20-4.58**	**.01**
Preoperative eGFR ≥60 mL/min/1.73 m^2	**0.55**	**0.33-0.91**	**.02**	1.47	0.73-2.97	.29
Hospital stay ≥3 days	1.40	0.78-2.51	.26	1.27	0.57-2.85	.56
Tumor depth	1.77	0.93-3.37	.08	**2.56**	**1.03-6.48**	**.04**
Tumor anteroposterior location	1.36	0.76-2.45	.30	1.07	0.47-2.43	.88
Tumor polarity	1.49	0.80-2.76	.21	0.51	0.22-1.18	.12
Tumor stage >T1a	1.42	0.56-3.62	.46	1.97	0.71-5.45	.19
Multiple tumors treated	0.68	0.27-1.70	.41	1.07	0.35-3.33	.90
Hilar location	0.91	0.43-1.94	.81	1.89	0.86-4.18	.11

Comparison of Safety, Renal Function Outcomes and Efficacy of Laparoscopic and Percutaneous Radio Frequency Ablation of Renal Masses

Ezekiel E. Young, Scott M. Castle, Vladislav Gorbatiy and Raymond J. Leveillee*,†

From the Department of Urology, Division of Endourology, Laparoscopy, and Minimally Invasive Surgery, University of Miami, Miller School of Medicine, Miami, Florida



Conclusions: Laparoscopic and computerized tomography guided radio frequency ablation appear safe and effective with statistically equivalent rates of complications and recurrence.

Percutaneous Ablation of Renal Masses Measuring 3.0 cm and Smaller: Comparative Local Control and Complications After Radiofrequency Ablation and Cryoablation

Thomas D. Atwell[1]
Grant D. Schmit[1]
Stephen A. Boorjian[2]
Jay Mandrekar[3]
A. Nicholas Kurup[1]
Adam J. Weisbrod[1]
George K. Chow[2]
Bradley C. Leibovich[2]
Matthew R. Callstrom[1]
David E. Patterson[2]
Christine M. Lohse[4]
R. Houston Thompson[2]

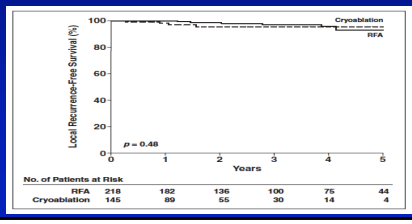


Fig. 1—Local recurrence-free survival for tumors treated with radiofrequency ablation (RFA) and cryoablation, including patients at risk.

ABLATIVE THERAPIES
Current limitations

Mainly retrospective series – short/intermediate follow-up

Lack of histology in a proportion of cases

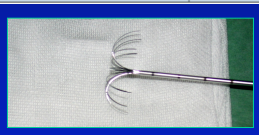
Risk of "tumor skipping"

Lack of standardized criteria to define treatment success

Limited data on long term oncological outcomes

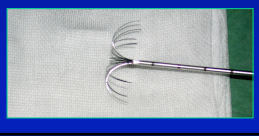
EAU Guidelines on Renal Cell Carcinoma

Recommendation	Strength rating
Offer active surveillance, radiofrequency ablation and cryoablation to elderly and/or comorbid patients with small renal masses.	Weak



EAU Guidelines on Renal Cell Carcinoma

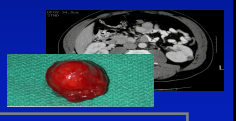
The quality of the available data does not allow any definitive conclusions regarding morbidity and oncological outcomes of cryoablation and radiofrequency ablation.	3
Low quality studies suggest a higher local recurrence rate for minimally invasive therapies compared to partial nephrectomy.	3



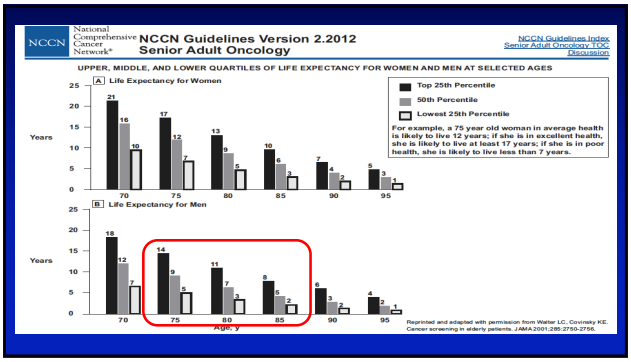
Patient selection

HOW TO SELECT PATIENTS FOR NON SURGICAL MANAGEMENT?

Patient features



Tumor features



BJUI

Can we avoid surgery in elderly patients with renal masses by using the Charlson comorbidity index?

Kevin M. O'Connor, Niall Davis, Gerry M. Lennon, David M. Quinlan and David W. Mulvin

Department of Urology, St. Vincent's University Hospital, Dublin, Ireland

Accepted for publication 25 September 2008

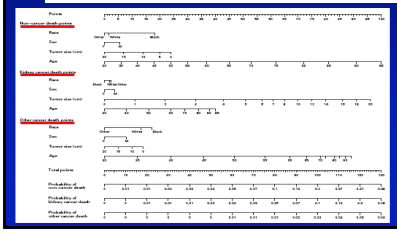
Elderly patients with small renal tumours (T1a) and comorbidity scores of ≥3 were more likely to die as a result of their comorbidities rather than the renal tumour.

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

J Clin Oncol 28:311-317. © 2009 by American Society of Clinical Oncology

Evaluating Overall Survival and Competing Risks of Death in Patients With Localized Renal Cell Carcinoma Using a Comprehensive Nomogram

Alexander Kutikov, Brian L. Egleston, Yu-Ning Wong, and Robert G. Uzzo

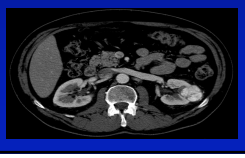


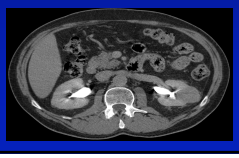
80 yo white male with a 1.6 cm ccRCC has:

20% 5y risk of non RCC death
16% 5y risk of other cancer death
2% 5y risk of RCC death

TRADITIONAL IMAGING

- High, but not excellent accuracy for the diagnosis of malignancy
- Poor ability to differentiate oncocytomas and "fat free" epitelioid angiomyolipomas





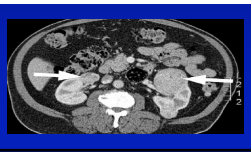
Renal oncocytoma: CT features cannot reliably distinguish oncocytoma from other renal neoplasms

Clinical Radiology (2009) 64, 517–522

S. Choudhary[a], A. Rajesh[a,*], N.J. Mayer[b], K.A. Mulcahy[a], A. Haroon[a]

Departments of [a]Radiology, and [b]Pathology, University Hospitals of Leicester NHS Trust, Leicester General Hospital, Leicester, UK

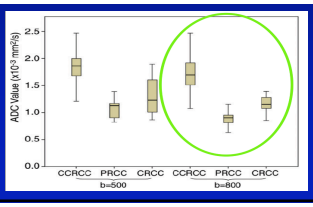
CONCLUSION: Renal oncocytoma is typically described as being hypervascular and homogeneous, with a characteristic central stellate scar on CT. The present study demonstrates that these imaging features are found in only a small proportion of these tumours. Therefore, imaging characteristics alone are unreliable when differentiating between oncocytoma and renal cell carcinoma, and histopathological diagnosis remains the reference standard.



DIFFUSION WEIGHTED MRI

Renal Cell Carcinoma: Diffusion-weighted MR Imaging for Subtype Differentiation at 3.0 T[1]

Wang et al Radiology 2010



In conclusion, clear cell and non–clear cell RCCs possess different diffusion characteristics that can be distinguished with high sensitivity and specificity when *b* values of 0 and 800 sec/mm² are used to calculate the ADC, potentially improving the accuracy of pretreatment diagnosis and selection of clinical therapy.

Contents lists available at ScienceDirect

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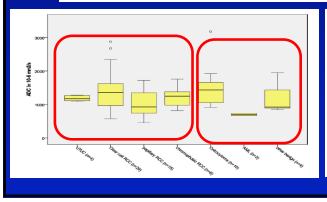
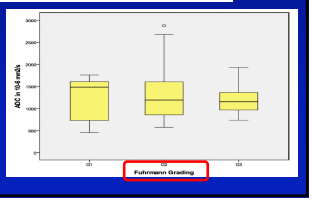
Utility and limitations of 3-Tesla diffusion-weighted magnetic resonance imaging for differentiation of renal tumors

S. Sevcenco[a,1], G. Heinz-Peer[b,2], L. Ponhold[b,2], D. Javor[b,2], F.E. Kuehhas[a,1], H.C. Klingler[a,1], M. Remzi[a,3], P. Weibl[a,1], S.F. Shariat[a,1], P.A. Baltzer[b,*]

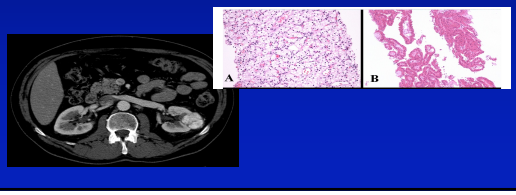
* Medical University of Vienna, Dept. of Urology, Waehringer Gürtel 18-20, 1090 Vienna, Austria
* Medical University of Vienna, Dept. of Biomedical Imaging and Image-guided Therapy, Waehringer Gürtel 18-20, 1090 Vienna, Austria





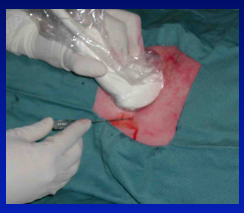
IMAGING

No significant ability to assess tumor aggressiveness



We need serum, urine or tissue markers of tumor aggressiveness

We need better histological definition by percutaneous needle biopsy



- Malignancy
- Histotype
- Grade
- Genetic and molecular characteristics

Rationale for Percutaneous Biopsy and Histologic Characterisation of Renal Tumours

Alessandro Volpe [a,], Antonio Finelli [b], Inderbir S. Gill [c], Michael A.S. Jewett [b], Guido Martignoni [d], Thomas J. Polascik [e], Mesut Remzi [f], Robert G. Uzzo [g]*

	No. of tumours biopsied	Image guidance	No. of significant complications (%)	No. of seeding (%)	No. of significant bleeding (%)
Neuzillet et al. [8]	88	CT	0	0	0
Shannon et al. [9]	235	CT/US	2 (0.9)	0	2 (0.9)
Schmidbauer et al. [10]	78	CT	1 (1.3)	0	0
Lebret et al. [11]	119	CT/US	0	0	0
Maturen et al. [12]	152	CT/US	2 (1.3)	0	2 (1.3)
Volpe et al. [13]	100	CT/US	1 (1)	0	0
Wang et al. [14]	110	CT/US	2 (1.8)	0	1 (0.9)
Veltri et al. [15]	150	US	0	0	0
Leveridge et al. [16]	345	CT/US	1 (0.3)	0	1 (0.3)

	No. of tumours biopsied	Diagnostic biopsies, %	Accuracy for malignancy, %	Accuracy for RCC subtyping, %	Accuracy for grading, %
Neuzillet et al. [8]	88	91	92	92	69.8
Shannon et al. [9]	235	78	100	98	NR
Schmidbauer et al. [10]	78	97	Sensitivity 93.5 Specificity 100	91	76
Lebret et al. [11]	119	79	86	86	46/74**
Maturen et al. [12]	152	96	Sensitivity 97.7 Specificity 100	NR	NR
Volpe et al. [13]	100	84	100	100	66.7/75**
Wang et al. [14]	110	90.9	100	96.6	NR
Veltri et al. [15]	103	100	NR	93.2	NR
Leveridge et al. [16]	345	80.6	99.7	88	63.5

ACCURACY OF RENAL TUMOR BIOPSY

Assessment of accuracy *is limited*

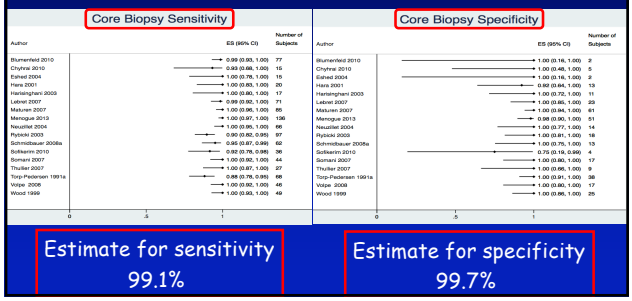
- Most studies are retrospective and single institutional
- Populations are different or mixed (SRMs – mRCC)
- Different biopsy schemes are used
- Lack of the ideal reference standard in many cases

Systematic Review and Meta-analysis of Diagnostic Accuracy of Percutaneous Renal Tumour Biopsy

Lorenzo Marconi [a], Saeed Dabestani [b], Thomas B. Lam [c], Fabian Hofmann [d], Fiona Stewart [c], John Norrie [e], Axel Bex [f], Karim Bensalah [g], Steven E. Canfield [h], Milan Hora [i], Markus A. Kuczyk [j], Axel S. Merseburger [k], Peter F.A. Mulders [l], Thomas Powles [m], Michael Staehler [n], Borje Ljungberg [o], Alessandro Volpe [p,]*

[a] Department of Urology, Coimbra University Hospital, Coimbra, Portugal; [b] Department of Urology, Skåne University Hospital, Malmö, Sweden; [c] Academic Urology Unit, University of Aberdeen, Aberdeen, UK; [d] Department of Urology, Sunderby Hospital, Sunderby, Sweden; [e] Health Services Research Unit, University of Aberdeen, UK; [f] Department of Urology, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands; [g] Department of Urology, University of Rennes, Rennes, France; [h] Division of Urology, University of Texas Medical School at Houston, Houston, TX, USA; [i] Department of Urology, Faculty Hospital and Faculty of Medicine in Pilsen, Charles University in Prague, Prague, Czech Republic; [j] Department of Urology and Urologic Oncology, Hannover Medical School, Hannover, Germany; [k] Department of Urology, University Hospital Schleswig-Holstein, Lübeck, Germany; [l] Department of Urology, Radboud University, Nijmegen, The Netherlands; [m] Barts Cancer Institute, Queen Mary University of London, St. Bartholomew's Hospital, London, UK; [n] Department of Urology, Ludwig-Maximilians University, Munich, Germany; [o] Department of Surgical and Perioperative Sciences, Urology and Andrology, Umed University, Umed, Sweden; [p] Division of Urology, Maggiore della Carità Hospital, University of Eastern Piedmont, Novara, Italy*

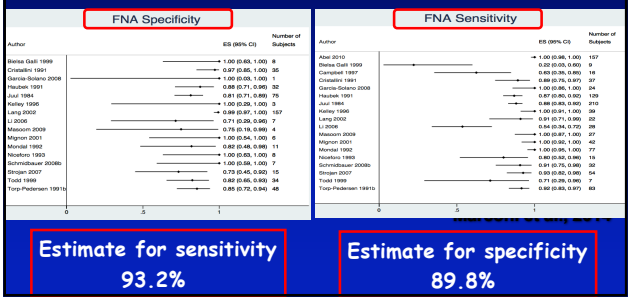
ACCURACY for MALIGNANCY



Estimate for sensitivity 99.1%

Estimate for specificity 99.7%

ACCURACY for MALIGNANCY



Estimate for sensitivity 93.2%

Estimate for specificity 89.8%

Rationale for Percutaneous Biopsy and Histologic Characterisation of Renal Tumours

Alessandro Volpe[a,], Antonio Finelli[b], Inderbir S. Gill[c], Michael A.S. Jewett[b], Guido Martignoni[d], Thomas J. Polascik[e], Mesut Remzi[f], Robert G. Uzzo[g]*

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Leveridge et al. [16]	345	80.6	99.7	88	63.5

SYSTEMATIC REVIEW

Median concordance rate 90.3% (96% for SRMs)

Can Renal Biopsy Accurately Predict Histological Subtype and Fuhrman Grade of Renal Cell Carcinoma?

Ingrid Millet, Fernanda Curros, Isabelle Serre, Patrice Taourel* and Rodolphie Thuret

Biopsy performance for tumor			
No. RCC with Grading Possible	% Accurate Diagnosis	% Accurate Diagnosis Low Grade/High Grade	References
52	70	80	Neuzillet et al[13]
52	46	74	Lebret et al[10]
67	43	64	Blumenfeld et al[26]
12	66	75	Volpe et al[14]
46		66	Ficarra et al[28]
61	75	93	Present series

SYSTEMATIC REVIEW

median concordance rate

62.5% (4-tier system) -> 87% (2-tier system)

PRECISION MEDICINE

Precision medicine is a medical model that proposes the customization of healthcare with medical decisions, treatment and practices tailored to the individual patient

Diagnostic testing is employed for selecting appropriate and optimal therapies based on genetic or other molecular or cellular analysis, imaging and analytics

PRECISION MEDICINE in RCC

HIGH RISK/ADVANCED/METASTATIC DISEASE

- Indications for adjuvant therapy after nephrectomy
- Indications for cytoreductive nephrectomy in mRCC
- Selection of the optimal targeted / IO therapy

LOCALIZED DISEASE

- Indications for non-surgical management in select patients
- Indications for NSS in larger tumors (T1b-T2)
- Indications for lymph node dissection in high-risk disease

Guidelines on
Renal Cell Carcinoma

B. Ljungberg (chair), K. Bensalah, A. Bex (vice-chair), S. Canfield, S. Dabestani, F. Hofmann, M. Hora, M.A. Kuczyk, T. Lam, L. Marconi, A.S. Merseburger, P.F.A. Mulders, T. Powles, M. Staehler, A. Volpe

RENAL TUMOR BIOPSY

Perform a renal tumour biopsy before ablative therapy and systemic therapy without previous pathology.	Strong
Perform a percutaneous biopsy in select patients who are considered for active surveillance.	Weak
Use a coaxial technique when performing a renal tumour biopsy.	Strong
Do not perform a renal tumour biopsy of cystic renal masses.	Strong
Use a core biopsy technique rather than fine needle aspiration for histological characterisation for solid renal tumours.	Strong

EASE TRANSLATIONAL STUDY OBJECTIVES

To identify clinical and pathological prognostic factors of fast growth rate and progression for small RCCs

To identify tissue, serum and urine molecular and genetic predictive biomarkers of fast growth and progression of small RCCs

RCC HETEROGENEITY

CLINICAL HETEROGENEITY

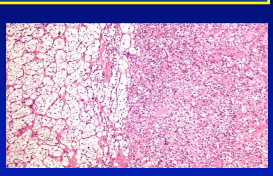
HISTOLOGICAL HETEROGENEITY
- Intertumoral / Intratumoral
- Histotype / Grade

MOLECULAR GENETIC HETEROGENEITY
- Intertumoral / Intratumoral

INTRATUMORAL HETEROGENEITY

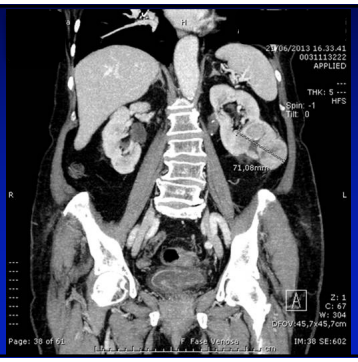
The slides of 43 <3 cm surgically removed ccRCCs were reviewed by a single GU pathologist

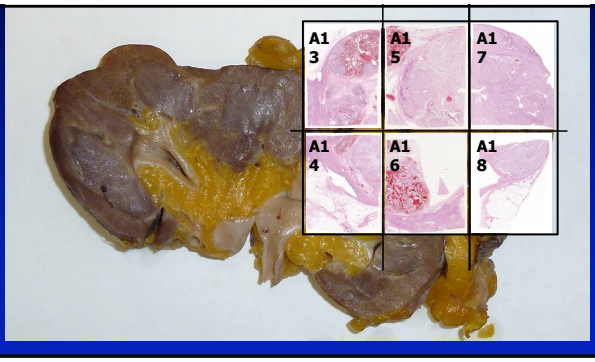
The presence of Fuhrman grade heterogeneity (I-II vs. III-IV) in different areas of the same tumor was assessed

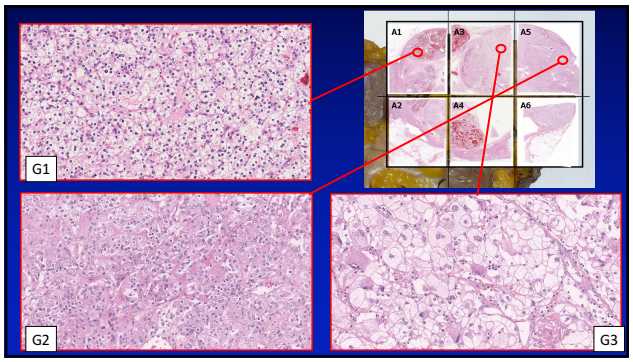


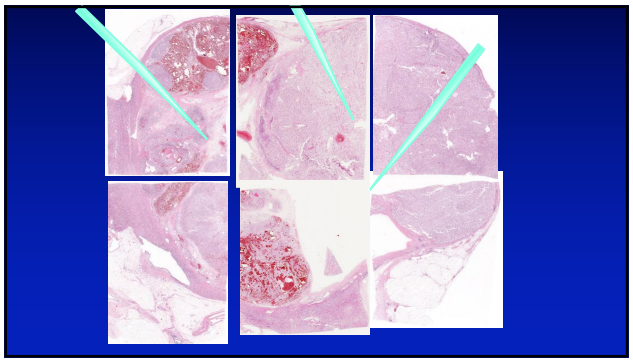
7/43 tumors (16%)
intratumoral heterogeneity

Volpe and Jewett, unpublished data, 2004









The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 8, 2012 VOL. 366 NO. 10

Intratumor Heterogeneity and Branched Evolution Revealed by Multiregion Sequencing

Marco Gerlinger, M.D., Andrew J. Rowan, B.Sc., Stuart Horswell, M.Math., James Larkin, M.D., Ph.D., David Endesfelder, Dip.Math., Eva Gronroos, Ph.D., Pierre Martinez, Ph.D., Nicholas Matthews, B.Sc., Aengus Stewart, M.Sc., Patrick Tarpey, Ph.D., Ignacio Varela, Ph.D., Benjamin Phillimore, B.Sc., Sharmin Begum, M.Sc.,

CONCLUSIONS

Intratumor heterogeneity can lead to underestimation of the tumor genomics landscape portrayed from single tumor-biopsy samples and may present major challenges to personalized-medicine and biomarker development. Intratumor heterogeneity, associated with heterogeneous protein function, may foster tumor adaptation and therapeutic failure through Darwinian selection. (Funded by the Medical Research Council and others.)

BIOPSY PATTERN

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Vol. 171, 1802–1805, May 2004
Printed in U.S.A.
DOI: 10.1097/01.ju.0000120147.51090.2b

ACCURACY AND CLINICAL ROLE OF FINE NEEDLE PERCUTANEOUS BIOPSY WITH COMPUTERIZED TOMOGRAPHY GUIDANCE OF SMALL (LESS THAN 4.0 CM) RENAL MASSES

YANN NEUZILLET, ERIC LECHEVALLIER, MARC ANDRE, LAURENT DANIEL AND CHRISTIAN COULANGE

From the Department of Urology, Hospital Salvator (YN, EL, CC), and Departments of Radiology (MA) and Pathology (LD), Hospital de la Timone, Marseille, France

previous study.[4] In this study we checked the quality of the core. If core length was less than 10 mm or the core was torn we performed another biopsy. At least 2 whole core biopsies per tumor were obtained. In our current series of solid renal

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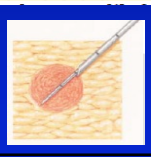
Vol. 174, 44–46, July 2005
Printed in U.S.A.
DOI: 10.1097/01.ju.0000162063.86400.de

THE ACCURACY OF 250 FINE NEEDLE BIOPSIES OF RENAL TUMORS

HEIKO WUNDERLICH,* WINFRIED HINDERMANN, AL MOHANNAD AL MUSTAFA, OLAF REICHELT, KERSTIN JUNKER AND JÖRG SCHUBERT

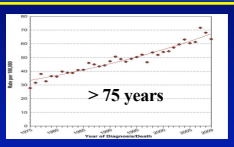
From the Department of Urology and the Institute of Pathology (WH), Friedrich-Schiller-University, Jena, Germany

sults we recommend 1 central and 1 peripheral biopsy in patients with renal lesions 4 cm or less in diameter and 2 peripheral biopsies guided by ultrasound in cases with renal tumors more than 4 cm in diameter. Since the larger the

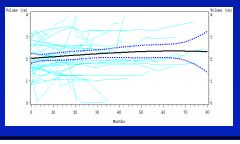


MANAGEMENT OF SRMs

The diagnosis of renal masses is increasing especially in the elderly population



A significant number of cT1 renal masses are benign tumors or RCCs with low aggressiveness



MANAGEMENT OF SRMs

Partial nephrectomy is the gold standard treatment

Radical nephrectomy is a reasonable choice in selected elderly patients with complex SRMs and normal preoperative renal function

Non surgical management should be discussed with elderly and comorbid patients with limited life expectancy and increased perioperative risk

MANAGEMENT OF SRMs

Percutaneous biopsy should be increasingly used for decision making in elderly and comorbid patients with SRMs

Randomized studies or long term results of well designed prospective studies have the potential to better define the best management of SRMs in elderly/comorbid patients

MANAGEMENT OF SRMs IN ELDERLY AND COMORBID PATIENTS

Percutaneous biopsy should be increasingly used for decision making in elderly and comorbid patients with SRMs

Randomized studies or long term results of well designed prospective studies have the potential to better define the best management of SRMs in elderly/comorbid patients