Franziskus-Krankenhaus Berlin

Beste Medizin und Menschlichkeit

Nierenzellkarzinom – Nierenkonservierende Therapie

PD Dr. Carsten Kempkensteffen
Klinik für Urologie
Franziskus-Krankenhaus Berlin

Berliner DialyseSeminar

Elisabeth Vinzenz Verbund

Das Franziskus-Krankenhaus Berlin gehört zum Elisabeth Vinzenz Verbund – einer starken Gemeinschaft katholischer Krankenhäuser, die für Qualität und Zuwendung in Medizin und Pflege stehen.

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Darlegung potentieller Interessenskonflikte

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Der Inhalt des folgenden Vortrages ist Ergebnis des Bemühens um größtmögliche Objektivität und Unabhängigkeit.

Als Referent versichere ich, dass in Bezug auf den Inhalt des folgenden Vortrags **keine Interessenskonflikte** bestehen, die sich aus einem Beschäftigungsverhältnis, einer Beratertätigkeit oder Zuwendungen für Forschungsvorhaben, Vorträge oder andere Tätigkeiten ergeben.

Agenda

- **Epidemiologie des Nierenzellkarzinoms**
- **TNM-Klassifikation**
- **Verteilung der Tumorstadien**
- **Datenlage: Partielle Nephrektomie (PN) vs Radikale Nephrektomie (RN)**
- **Prädiktion der postoperativen Nierenfunktion**
- **Alternativen zur operativen Therapie**
- **Fazit**

Epidemiologie des Nierenzellkarzinoms

- EU 2018: 100.000 Neudiagnosen und 40.000 Todesfälle
- Verhältnis Männer : Frauen = 1,5 : 1
- Höchste Inzidenz: 60. – 70. Lebensjahr
- Risikofaktoren (nicht modifizierbar / modifizierbar):
  - ✓Pos. Familienanamnese
  - ✓Terminale Niereninsuffizienz / Erworbene zyst. Nierendegeneration (ACKD)
  - ✓Heriditäre Tumorsyndrome (z.B. VHL-Syndrom)

  - ✓Nikotinabusus
  - ✓Adipositas
  - ✓Hypertonus

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TNM-Klassifikation

T - Primary Tumour		
TX	Primary tumour cannot be assessed	
T0	No evidence of primary tumour	
T1	Tumour ≤ 7 cm or less in greatest dimension, limited to the kidney	
	T1a	Tumour ≤ 4 cm or less
	T1b	Tumour > 4 cm but ≤ 7 cm
T2	Tumour > 7 cm in greatest dimension, limited to the kidney	
	T2a	Tumour > 7 cm but ≤ 10 cm
	T2b	Tumours > 10 cm, limited to the kidney
T3	Tumour extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota fascia	
	T3a	Tumour grossly extends into the renal vein or its segmental (muscle-containing) branches, or tumour invades perirenal and/or renal sinus fat (peripelvic fat), but not beyond Gerota fascia
	T3b	Tumour grossly extends into the vena cava below diaphragm
	T3c	Tumour grossly extends into vena cava above the diaphragm or invades the wall of the vena cava
T4	Tumour invades beyond Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)	

Verteilung T-Stadien Deutschland

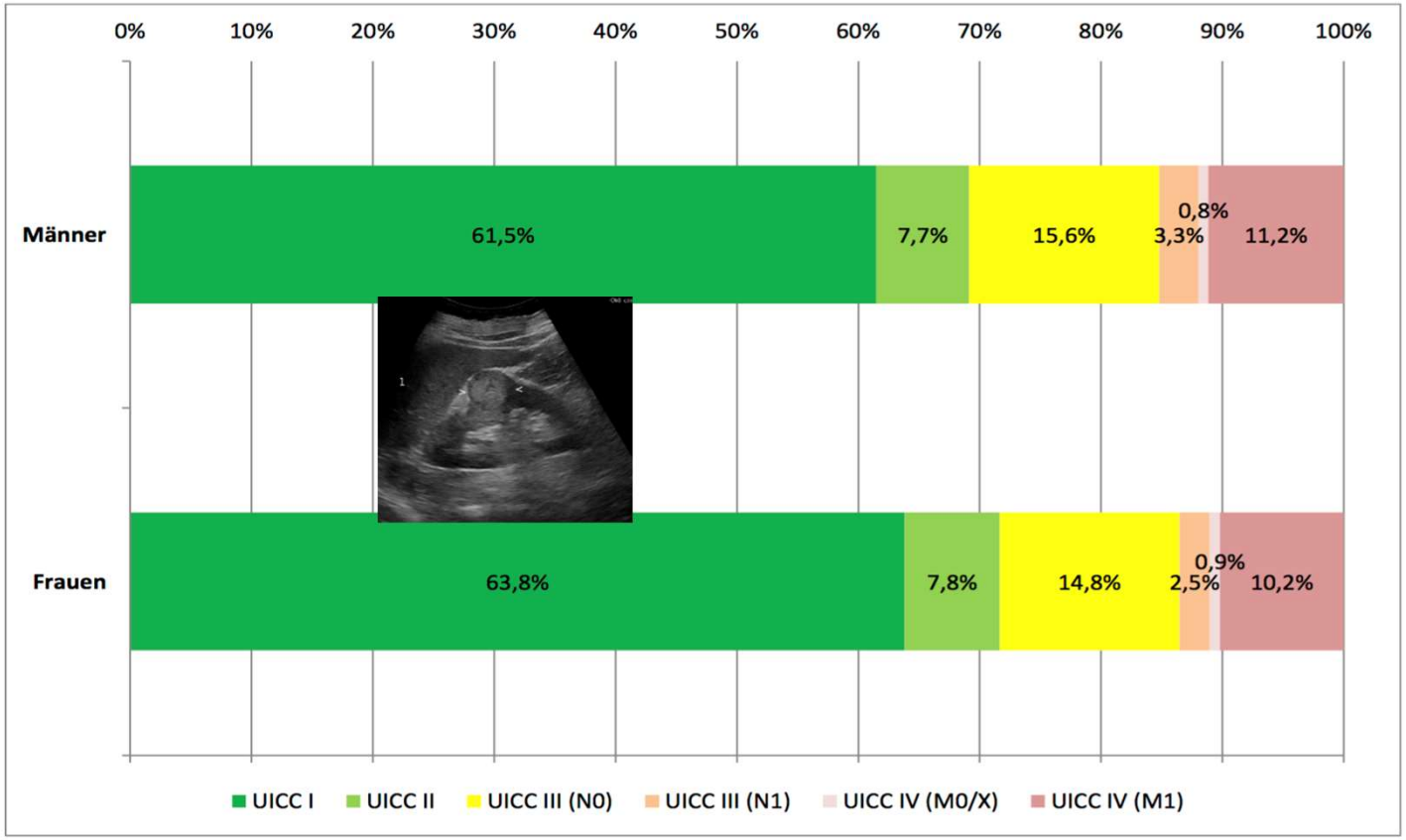

Abbildung 3: Verteilung der UICC-Stadien bei Erstdiagnose eines Nierenzellkarzinoms in Deutschland 2012 bis 2014, nach Geschlecht.

EAU Leitlinie 2020

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

Summary of evidence	LE
The oncological outcome in terms of OS following PN equals that of RN in patients with c/p T1 RCC.	1b

<u>Hypothese:</u>

Bei onkologischer Gleichwertigkeit von partieller Nephrektomie (PN) und radikaler Nephrektomie (RN) OS Vorteil der PN durch:

- ✓geringere Rate an postoperativer Niereninsuffizienz
- ✓geringere kardiovaskuläre Mortalität

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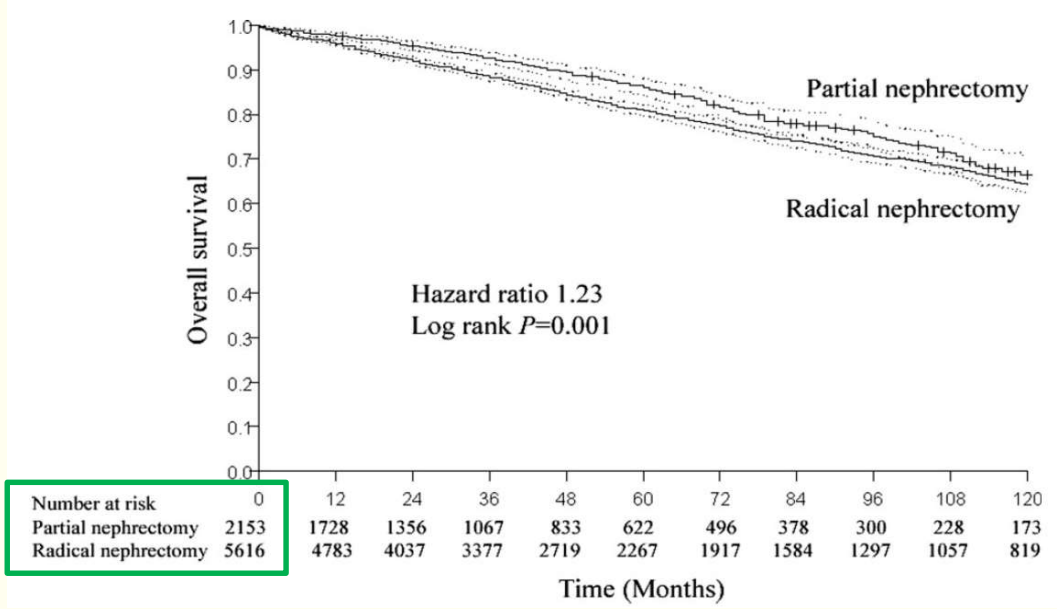
PN versus RN

Radical Versus Partial Nephrectomy

Effect on Overall and Noncancer Mortality

Laurent Zini, MD, PhD[1,2], Paul Perrotte, MD[3], Umberto Capitanio, MD[1,4], Claudio Jeldres, MD[1],



Number at risk	0	12	24	36	48	60	72	84	96	108	120
Partial nephrectomy	2153	1728	1356	1067	833	622	496	378	300	228	173
Radical nephrectomy	5616	4783	4037	3377	2719	2267	1917	1584	1297	1057	819

RN: 23% erhöhtes, relatives Gesamtmortalitätsrisiko
4.9% erhöhtes, absolutes Gesamtmortalitätsrisko nach 5 J.

Cancer; 2009

Stand 1911

PN versus RN

Kidney Cancer

Radical Versus Partial Nephrectomy for cT1 Renal Cell Carcinoma

Boris Gershman [a,b,], R. Houston Thompson [c], Stephen A. Boorjian [c], Christine M. Lohse [d], Brian A. Costello [e], John C. Cheville [f], Bradley C. Leibovich [c]*

Table 2 – Comparisons of clinical, radiographic, and pathologic features by the type of nephrectomy in the pseudo cohort of patients with RCC after reweighting by stabilized IPWs

Feature	PN (N = 919)	RN (N = 690)	p value
Preoperative clinical and radiographic features			
Year of surgery	2003 (1998–2006)	2002 (1998–2006)	0.5
Age at surgery (yr)	65 (55–72)	64 (57–72)	0.8
Charlson score	1 (0–2)	1 (0–2)	0.7
BMI (kg/m^2)	28.6 (25.7–32.6)	29.4 (25.9–32.9)	0.9
Preoperative eGFR	65.8 (53.8–75.9)	64.4 (53.7–76.2)	0.4
Tumor size (cm)	3.8 (2.5–5.0)	3.6 (2.5–5.0)	0.7

Eur Urol; 2018

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PN versus RN

Kidney Cancer

Radical Versus Partial Nephrectomy for cT1 Renal Cell Carcinoma

Boris Gershman [a,b,], R. Houston Thompson [c], Stephen A. Boorjian [c], Christine M. Lohse [d], Brian A. Costello [e], John C. Cheville [f], Bradley C. Leibovich [c]*

Table 3 – Associations of the type of nephrectomy with oncologic and nononcologic outcomes in the subset of patients with RCC after further adjustment for pathologic features

Outcome	HR[a] (95% CI)	*p* value
Cancer-specific mortality		
Adjusted for PS quintile	1.08 (0.64–1.81)	0.8
Stratified by PS quintile	1.00 (0.57–1.77)	0.9
In pseudo cohort after reweighting by stabilized IPWs	1.05 (0.66–1.65)	0.8
In subset of 363 matched pairs	1.40 (0.72–2.72)	0.3
All-cause mortality		
Adjusted for PS quintile	1.14 (0.94–1.38)	0.2
Stratified by PS quintile	1.15 (0.95–1.39)	0.2
In pseudo cohort after reweighting by stabilized IPWs	1.18 (1.01–1.38)	0.03
In subset of 363 matched pairs	1.14 (0.91–1.44)	0.3
Other-cause mortality		
Adjusted for PS quintile	1.14 (0.91–1.42)	0.3
Stratified by PS quintile	1.17 (0.94–1.46)	0.2
In pseudo cohort after reweighting by stabilized IPWs	1.17 (0.98–1.40)	0.08
In subset of 363 matched pairs	1.10 (0.85–1.43)	0.5

Eur Urol; 2018

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PN versus RN

Comparison of Partial Versus Radical Nephrectomy Effect on Other-cause Mortality, Cancer-specific Mortality, and 30-day Mortality in Patients Older Than 75 Years

Michele Marchioni [a,b,], Felix Preisser [a,c], Marco Bandini [a,d,e], Sebastiano Nazzani [a,f], Zhe Tian [a]*

Table 1 – Clinical and pathologic characteristics of patients older than 75 yr with pT1a renal cell carcinoma, stratified according to partial and radical nephrectomy status before and after propensity score matching.

Variables	Before propensity score matching				After propensity score matching			
	Overall *N* = 4541	Radical nephrectomy *N* = 2650 (58.4)	Partial nephrectomy *N* = 1891 (41.6)	*p* value	Overall *N* = 2826	Radical nephrectomy *N* = 1413 (50.0)	Partial nephrectomy *N* = 1413 (50.0)	*p* value
Age at diagnosis (yr)	78 (76–81)	79 (76–82)	78 (76–80)	<0.001	78 (76–81)	78 (76–81)	78 (76–81)	0.6
Size (according to the median size)				<0.001				1
Small (≤3.0 cm)	2714 (59.8)	1365 (51.5)	1349 (71.3)		1851 (65.5)	925 (65.5)	926 (65.5)	
Large (>3.0 cm)	1827 (40.2)	1285 (48.5)	542 (28.7)		975 (34.5)	488 (34.5)	487 (34.5)	

Eur Urol Focus; 2018

Stand 1911

PN versus RN

Comparison of Partial Versus Radical Nephrectomy Effect on Other-cause Mortality, Cancer-specific Mortality, and 30-day Mortality in Patients Older Than 75 Years

Michele Marchioni [a,b,], Felix Preisser [a,c], Marco Bandini [a,d,e], Sebastiano Nazzani [a,f], Zhe Tian [a]*

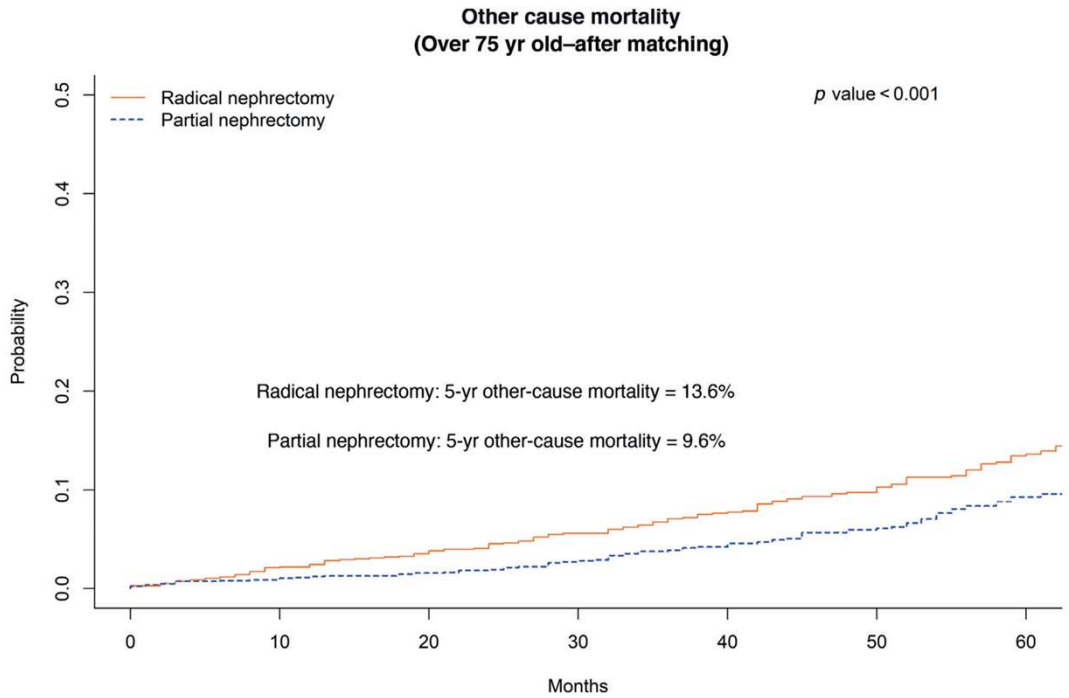

Fig. 2 – Propensity score–matched cumulative incidence plots depicting other-cause mortality rates after adjustment for cancer-specific mortality and stratified according to nephrectomy type.

Eur Urol Focus; 2018

Stand 1911

PN versus RN

Comparison of partial vs radical nephrectomy with regard to other-cause mortality in T1 renal cell carcinoma among patients aged ≥75 years with multiple comorbidities

Maxine Sun*, Marco Bianchi*†, Quoc-Dien Trinh*‡, Jens Hansen*§, Firas Abdollah†,

Variable	Overall	Pre-propensity matching			Post-propensity matching		
		PN	RN	Standardized mean differences	PN	RN	Standardized mean differences
No. of patients (%)	7524	924 (8.3)	6600 (87.7)	–	924 (50)	924 (50)	–
Age, years				−0.370			0.035
Mean (median)	75 (76)	74 (74)	76 (76)		74 (74)	73 (73)	
Interquartile range	71–79	69–78	71–79		69–78	69–77	
Tumour size, cm				−0.832			−0.016
Mean (median)	3.9 (3.8)	2.9 (2.7)	4.0 (4.0)		2.9 (2.7)	2.9 (2.8)	
Interquartile range	2.7–5.0	2.0–3.5	3.0–5.0		2.0–3.5	2.0–3.6	
Tumour stage, *n* (%)				−0.781			−0.027
T1a	4536	784 (85)	3752 (57)		784 (85)	775 (84)	
T1b	2988	140 (15)	2848 (43)		140 (15)	149 (16)	
Baseline hypercalcaemia, *n* (%)	152	20 (2)	132 (2)	0.011	20 (2)	19 (2)	0.007
Baseline hyperlipidaemia, *n* (%)	4492	681 (74)	3811 (58)	0.362	681 (74)	676 (73)	0.012
Baseline anaemia, *n* (%)	2864	342 (37)	2522 (38)	−0.025	342 (37)	343 (37)	−0.002

BJU Int; 2013

Stand 1911

PN versus RN

Comparison of partial vs radical nephrectomy with regard to other-cause mortality in T1 renal cell carcinoma among patients aged ≥75 years with multiple comorbidities

Maxine Sun*, Marco Bianchi*†, Quoc-Dien Trinh*‡, Jens Hansen*§, Firas Abdollah†,

Table 2 Association between treatment type (PN vs RN) and OCM in the post-propensity matched cohort and subgroups*.

	PN vs RN HR (95% CI)	*P*
Entire population	0.84 (0.70–0.98)	0.048
Subgroups		
≥75 years old	0.83 (0.65–1.07)	0.16
≥2 baseline comorbidities	0.83 (0.67–1.03)	0.10
≥75 years and ≥2 baseline comorbidities	0.77 (0.54–1.10)	0.15

**All models adjusted for cancer-specific mortality, patient age, year at surgery, race, sex, marital status, SES, population density, baseline comorbidities, tumour stage, tumour size, baseline hyperlipidaemia, baseline hypercalcaemia, and baseline anaemia.*

Schlussfolgerung:

-Patienten ≥ 75J.

<u>und / oder</u>

-Patienten mit ≥ 2 Komorbiditäten

profitieren im Hinblick auf die Gesamtmortalität nicht von einer PN

BJU Int; 2013

Stand 1911

PN versus RN

Kidney Cancer

Radical Versus Partial Nephrectom

Boris Gershman [a,b,], R. Houston Thompson [c], Step*
Brian A. Costello [e], John C. Cheville [f], Bradley C. Le

Comparison of partial vs
with regard to other-caus
cell carcinoma among p
years with multiple como

Maxine Sun*, Marco Bianchi*†, Quoc-Dien

Partial Nephrectomy

er Mortality

ID[3], Umberto Capitanio, MD[1,4], Claudio Jeldres, MD[1],

s Radical Nephrectomy Effect on
er-specific Mortality, and 30-day
Than 75 Years

Marco Bandini [a,d,e], Sebastiano Nazzani [a,f], Zhe Tian [a]

Retrospektive Analysen
(SEER-Datenbank)

PN versus RN

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

Med. FU 9,3 J.

Hendrik Van Poppel [a,], Luigi Da Pozzo [b,1], Walter Albrecht [c], Vsevolod Matveev [d],*

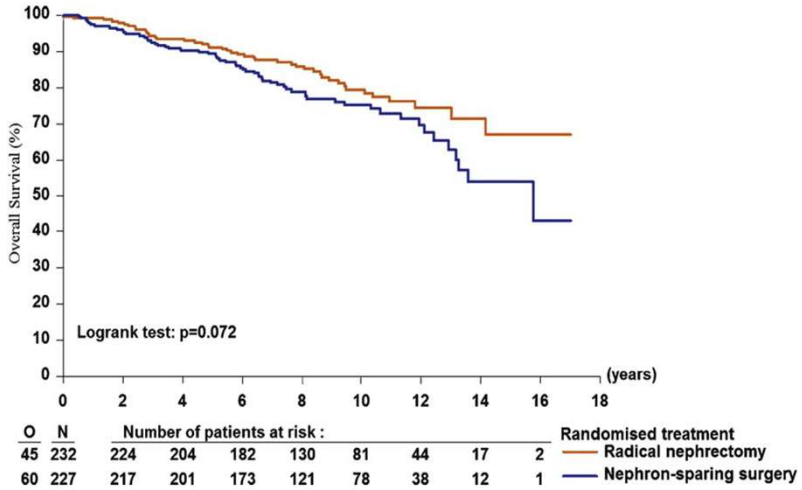

Fig. 3 – Kaplan-Meier estimates with log-rank test for overall survival in renal cell carcinoma patients after nephron-sparing surgery and radical nephrectomy.

Table 5 – Survival status and cause of death

	RN (n = 273)	NSS (n = 268)	Total (n = 541)
Survival status no. (%)			
Alive	198 (72.5)	173 (64.6)	371 (68.6)
Dead	50 (18.3)	67 (25.0)	117 (21.6)
Lost to follow-up	25 (9.2)	28 (10.4)	53 (9.8)
Alive/lost to follow-up, no. (%)	223 (81.7)	201 (75.0)	424 (78.4)
Cause of death, no. (%)			
Liver related	0 (0.0)	4 (1.5)	4 (0.7)
Renal related	4 (1.5)	8 (3.0)	12 (2.2)
Surgery related	1 (0.4)	2 (0.7)	3 (0.6)
Infection	3 (1.1)	2 (0.7)	5 (0.9)
Cardiovascular death	20 (7.3)	25 (9.3)	45 (8.3)
Chronic pulmonary disease	2 (0.7)	3 (1.1)	5 (0.9)
Second primary	7 (2.6)	11 (4.1)	18 (3.3)
Natural	5 (1.8)	2 (0.7)	7 (1.3)
Other (not chronic renal disease)	3 (1.1)	7 (2.6)	10 (1.8)
Unknown	5 (1.8)	3 (1.1)	8 (1.5)

RN = radical nephrectomy; NSS = nephron-sparing surgery.

cave: nur 541 von geplanten 1.300 Patienten randomisiert

Eur Urol; 2011

Stand 1911

PN versus RN

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]*

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 <45	127	49.0	69	27.1	21.9	(13.8–30.2)	
	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	(11.8–28.7)	<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.

Eur Urol; 2014

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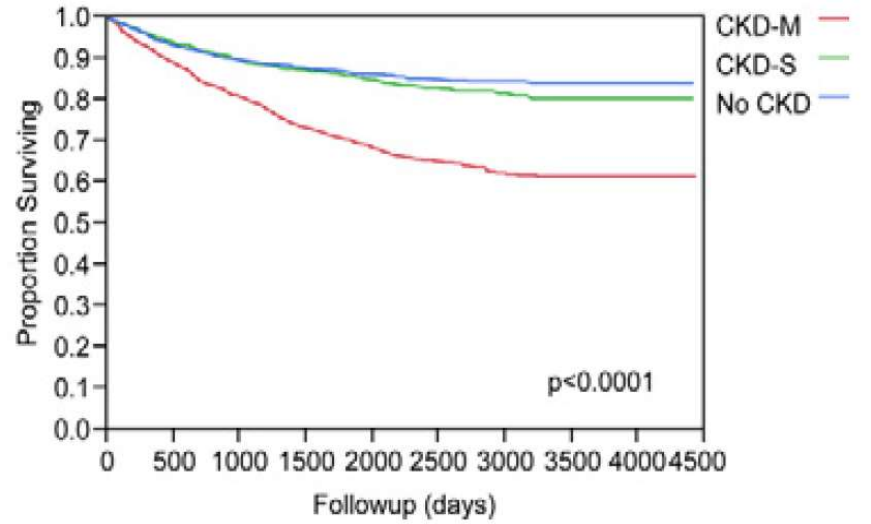
PN versus RN

Surgically induced chronic kidney disease may be associated with a lower risk of progression and mortality than medical chronic kidney disease

Brian R Lane [1], Steven C Campbell, Sevag Demirjian, Amr F Fergany



- 4.180 Pat.; med. FU 6,6 J.
- **CKD-M** 28% prä-OP GFR < 60ml/min
- **CKD-S** 22% de novo GFR < 60ml/min

Erhöhung des Mortalitätsrisikos post-OP:

prä-OP CKD-Stad. 3:	1,8-fach
prä-OP CKD-Stad. 4:	3,5-fach
prä-OP CKD-Stad. 5:	4,4-fach

Schlussfolgerungen:

- CKD OP-bdg. : geringes Progressionsrisiko; Mortalität nicht signif. erhöht.
- CKD prä-OP durch Vorerkrankungen: hohes Progressionsrisiko, Mortalitiät signif. erhöht.

J Urol; 2013

Stand 1911

PN versus RN

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

Med. FU 9,4 J.

Brian R. Lane [a], Sevag Demirjian [b], Ithaar H. Derweesh [c], Toshio Takagi [b], Zhiling Zhang [b,d],

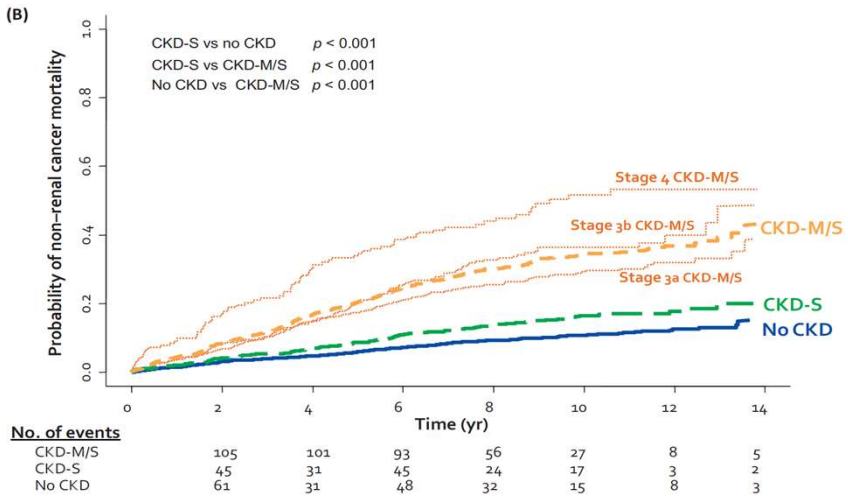


Fig. 2 – (A) All-cause mortality and (B) non–renal cancer mortality after renal cancer surgery according to CKD group. There are significant differences ($p < 0.001$) between patients with no CKD, CKD-S, and CKD-M/S. The CKD-M/S cohort is further subdivided into those with stage 3a ($n = 715$, 45–59 ml/min/1.73 m^2), stage 3b ($n = 366$, 30–44 ml/min/1.73 m^2), and stage 4 ($n = 153$, 15–29 ml/min/1.73 m^2) CKD. CKD = chronic kidney disease; CKD-S = CKD due to surgical removal of nephrons; CKD-M/S = CKD due to medical and surgical causes.

Schlussfolgerung:

- CKD prä-OP: erhöhtes Mortalitätsrisiko; Organerhalt anstreben, wenn technisch möglich.

Eur Urol; 2015

PN versus RN

Predicting Renal Function Outcomes After Partial and Radical Nephrectomy

Bimal Bhindi [a,b], Christine M. Lohse [c], Phillip J. Schulte [c], Ross J. Mason [a], John C. Cheville [d], Stephen A. Boorjian [a], Bradley C. Leibovich [a], R. Houston Thompson [a,]*

Table 2 – Multivariable models to predict long-term eGFR

Feature	Estimate	SE	*p* value
PN			
Intercept	31.8	2.69	<0.001
Age (yr)	−0.221	0.0302	<0.001
Solitary kidney	−6.87	1.16	<0.001
Diabetes	0.685	0.880	0.4
Hypertension	−1.79	0.613	0.004
Preoperative eGFR (ml/min/1.73 m^2)	0.741	0.0176	<0.001
Proteinuria			
None/mild	Reference		
Moderate	−1.84	0.792	0.02
Severe	−5.92	1.14	<0.001
Minimally invasive approach (vs open)	3.05	0.664	<0.001
Time from surgery (mo)	0.164	0.0455	<0.001
Age × time from surgery	−0.0017	0.0005	0.001
Diabetes × time from surgery	−0.0781	0.0150	<0.001
Preoperative eGFR × time from surgery	−0.0012	0.0003	<0.001
Proteinuria × time from surgery			
None/mild	Reference		
Moderate	−0.0315	0.0131	0.02
Severe	−0.110	0.0196	<0.001

Table 2 – Multivariable models to predict long-term eGFR

Feature	Estimate	SE	*p* value
RN			
Intercept	29.8	2.90	<0.001
Age (yr)	−0.235	0.0309	<0.001
Diabetes	−3.30	0.950	<0.001
Preoperative eGFR (ml/min/1.73m^2)	0.457	0.0202	<0.001
Preoperative proteinuria			
None/mild	Reference		
Moderate	−1.39	0.808	0.08
Severe	−4.26	1.02	<0.001
Tumor size (cm)	0.401	0.0909	<0.001
Time from surgery (mo)	0.148	0.0322	<0.001
Age × time from surgery	−0.0020	0.0005	<0.001

Eur Urol; 2019

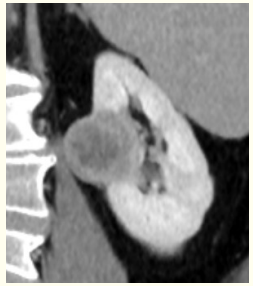
Stand 1911

PN versus RN

Renal Function Outcomes Following Radical or Partial Nephrectomy for Localized Renal Cell Carcinoma: Should Urologists Rely on Preoperative Variables to Predict Renal Function in the Long Term?

*Ardalan E. Ahmad *, Antonio Finelli*

Modell von Bhindi et al. nur mäßig prädiktiv für post-OP Nierenfunktion, da weitere signifikante Prädiktoren nicht inkludiert:



Tumorkomplexität (RENAL oder PADUA Score)

OP-Technik | Exzsionstechnik | Art/Dauer Ischämie | Qualität Operateurs

Quantität und Qualität des post-OP erhaltenen Nierengewebes

Eur Urol; 2019

Stand 1911

Organerhaltende Alternativen: EAU 2020

Aktive Überwachung und Thermische Ablationsverfahren:

Summary of evidence	LE
Most population-based analyses show a significantly lower cancer-specific mortality for patients treated with surgery compared to non-surgical management.	3
In active surveillance cohorts, the growth of small renal masses is low in most cases and progression to metastatic disease is rare (1-2%).	3
Quality of the available data does not allow definitive conclusions regarding morbidity and oncological outcomes of cryoablation and radiofrequency ablation.	3
Low quality studies suggest a higher local recurrence rate for thermal ablation therapies compared to partial nephrectomy.	3

Recommendation	Strength rating
Offer active surveillance, radiofrequency ablation or cryoablation to frail and/or comorbid patients with small renal masses.	Weak
When radiofrequency ablation, cryoablation and active surveillance are offered, inform patients about the higher risk of local recurrence and/or tumour progression.	Weak

EAU Guideline on RCC; 2020

Stand 1911

Fazit

- **Onkologische Gleichwertigkeit von PN und RN bei T1a Tumoren unstrittig.**
- **PN reduziert gegenüber RN das Risiko für die Entwicklung einer CKD.**
- **Datenlage bzgl. mögl. OS-Vorteil einer PN vs RN kontrovers.**
- **CKD-Pat. profitieren bzgl. OS wahrscheinlich am meisten von einer PN.**
- **RN bei Pat. mit normaler Nierenfunktion und komplexen Tumoren erwägen.**
- **AS bei Tu < 3cm und ablative Verfahren bei alten, komorbiden Pat. erwägen.**
- **Individuelle Beratung bzgl. Risiken und Chancen von PN vs RN unerlässlich.**

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Bleiben Sie gesund...

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