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DOES REDUCED RENAL FUNCTION PREDISPOSE TO CANCER MORTALITY DUE TO RCC?

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Introduction and Objectives

- Two recent publications reported an independent association between reduced renal function following nephrectomy and increased kidney cancer specific mortality*
- Authors suggested that PN should be prioritized whenever feasible to improve renal function and thereby potentially improve oncologic outcomes
- But is this correct, or will some patients be harmed with imprudent use of PN?

*Antonelli et al. European Urology (2018)
*Antonelli et al. Clinical Genitourinary Cancer (2019)

Introduction and Objectives

- **We hypothesized that this association might be related to confounding factors such as tumor characteristics rather than a direct effect of functional differences**

- **Objective:** to assess whether there is any independent association between preoperative or new-baseline eGFR and kidney cancer specific mortality (CSM) in patients undergoing PN or RN

Methods

Single-center retrospective review, all renal tumors managed with PN/RN (1999-2008, n = 4224)

Inclusion Criteria

- Pathological-confirmed RCC
- Available preoperative and new baseline eGFR values

Exclusion Criteria

- Non–RCC cases
- Previous PN/RN/TA for RCC
- Familial RCC
- Synchronous bilateral renal masses
- Renal vein or IVC involvement
- cT4, N1, M1 tumors

All cT1-T3a without renal vein involvement, N0,M0 RCC (n = 1394)

Cause-Specific Cox Proportional Hazard Regression Analysis

- **Primary Endpoint : Kidney Cancer-Specific Mortality**
- **Secondary Endpoints: Kidney Cancer Recurrence and Overall Survival**

Results

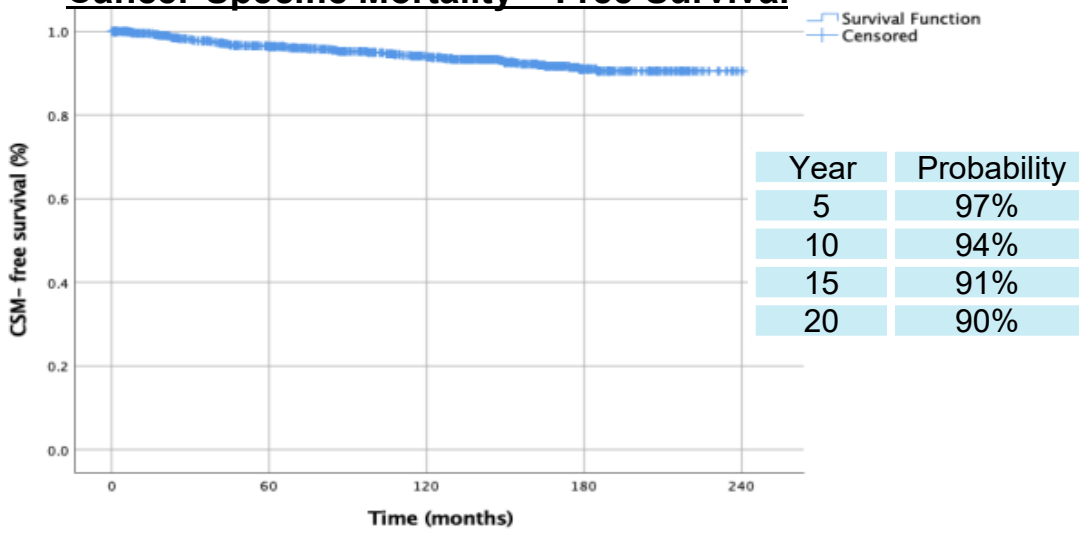
Demographics and Tumor Characteristics (PN= 867, RN=427):

Age (years), median (IQR)	60 (52-69)
Male, n (%)	897 (64)
Caucasians, n (%)	1208 (87)
BMI (kg/m^2), median (IQR)	29 (26-34)
Diabetes, n (%)	270 (19)
Hypertension, n (%)	835 (60)
Cardiovascular disease, n (%)	259 (19)
Coronary artery disease, n (%)	143 (10)
Chronic Kidney disease, n (%)	293 (21)
Smoking history, n (%)	629 (45)
ASA, median (IQR)	3 (2-3)
CCI, n (%)	
0	836 (60)
1	197 (14)
≥2	361 (26)
Symptomatic, n (%)	329 (24)
RENAL score, median (IQR)	7 (6-9)

Tumor size (cm), median (IQR)	3.5 (2.3-5.3)
pT stage, n (%)	
T1a	781 (56)
T1b	275 (20)
T2a	61 (4)
T2b	31 (2)
T3a	245 (18)
T4	1 (<1)
pN1 stage, n (%)	9 (<1)
Histology, n (%)	
Clear cell carcinoma	970 (70)
Papillary carcinoma	251 (18)
Chromophobe carcinoma	96 (7)
Other RCC	77 (5)
Sarcomatoid, n (%)	26 (2)
Rhabdoid, n (%)	8 (<1)
High Tumor grade (III/IV), n (%)	552 (40)
Tumor Necrosis, n (%)	362 (26)
Lymphovascular invasion, n (%)	57 (4)
Positive surgical margins, n (%)	34 (2)

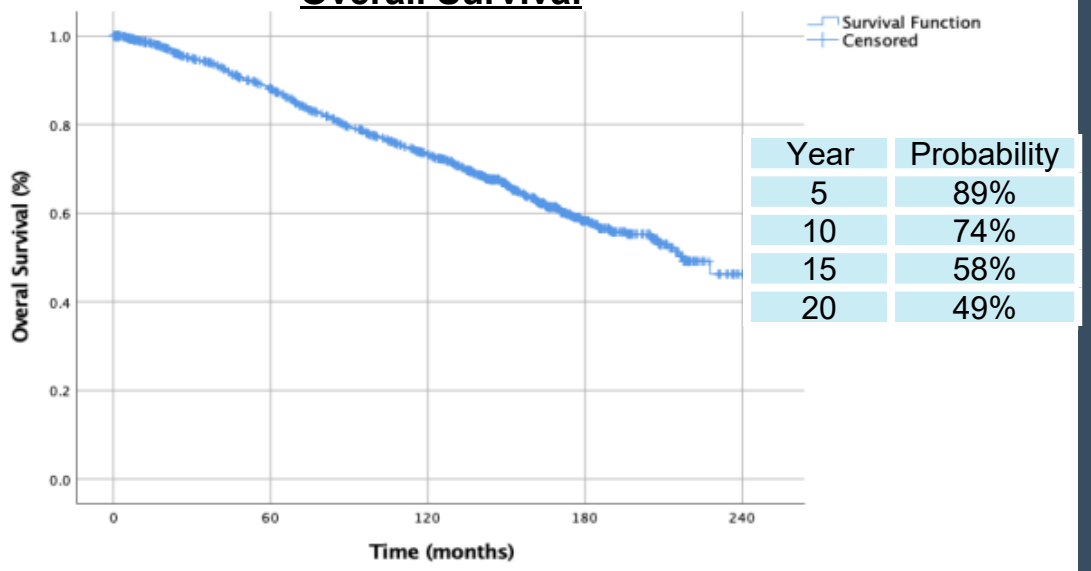
Survival Outcomes

Cancer-Specific Mortality – Free Survival



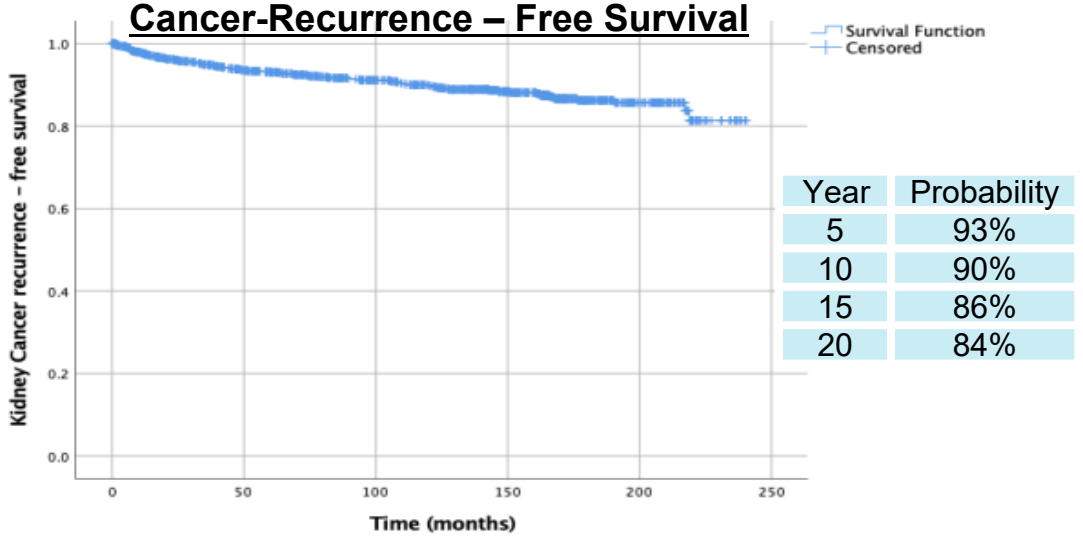
Year	Probability
5	97%
10	94%
15	91%
20	90%

Overall Survival



Year	Probability
5	89%
10	74%
15	58%
20	49%

Cancer-Recurrence – Free Survival



Year	Probability
5	93%
10	90%
15	86%
20	84%

- Median follow-up time among survivors was 11.91 years (IQR: 4.3 , 14.53)
- Overall 427 patients died and from those 79 patients died from kidney cancer
- 127 patients had kidney cancer recurrence

Functional Outcomes:

	Preoperative	New Baseline
eGFR (ml/min/1.73m^2), median (IQR)	80 (64-95)	60 (45-78)
CKD stage I-II (≥60 ml/min/1.73m^2), n (%)	1101 (79)	701 (50)
CKD stage III (30 – 59ml/min/1.73m^2), n (%)	260 (19)	582 (42)
CKD stage IV (15 – 30ml/min/1.73m^2), n (%)	30 (2)	80 (6)
CKD stage V (<15 ml/min/1.73m^2), n (%)	3 (<1)	30 (2)

Univariable Analysis	Cancer-Specific Mortality			Cancer Recurrence			Overall Survival		
	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
Preoperative GFR (per 10 units)	0.91	0.83,1.01	0.071	0.89	0.82-0.96	0.003	0.76	0.73,0.79	<0.01
New baseline GFR (per 10 units)	0.85	0.77,0.95	0.003	0.89	0.79-0.99	0.047	0.75	0.72,0.79	<0.01

Univariable Analysis for Kidney Cancer-Specific Mortality:

Characteristic	HR	95% CI	p-value
Age at nephrectomy	1.03	1.01, 1.05	0.006
Sex			0.13
Female	—		
Male	1.45	0.89, 2.36	
Pre-operative BMI	1.01	0.99, 1.05	0.53
Hypertension	1.71	1.05, 2.78	0.03
Diabetes	1.07	0.61, 1.88	0.81
Coronary artery disease	0.99	0.48, 2.06	0.98
Cardiovascular disease	0.73	0.38, 1.38	0.33
Surgery type			<0.001
Partial	—		
Radical	4.98	2.95, 8.43	
Tumor size	1.28	1.23, 1.34	<0.001
Pathologic stage			<0.001
Localized (pT1/2, N0, M0)	—		
Advanced (pT3+, N1)	3.72	2.38, 5.81	

Characteristic	HR	95% CI	p-value
Histology			0.002
Non- clear cell	—		
Clear cell	2.74	1.45, 5.18	
Tumor grade			<0.001
1,2	—		
3,4	4.98	2.95, 8.33	
Sarcomatoid	8.75	4.20,18.20	<0.001
Necrosis	3.30	2.12, 5.14	<0.001
LVI	2.49	1.14,5.40	0.02
Rhabdoid	12.03	3.78,38.28	<0.001
Margin status			0.98
Negative	—		
Positive	1.02	0.25, 4.14	

Multivariable Analysis

Variable	Cancer-Specific Mortality			Cancer Recurrence			Overall Survival		
	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
Age	1.03	1.00,1.06	0.03	1.01	0.99,1.03	0.22	1.05	1.04,1.06	<0.01
Sex			0.35			0.17			<0.01
Female	-			-			-		
Male	1.27	0.77,2.09		1.32	0.89,1.94		1.45	1.17,1.79	
Tumor size	1.25	1.20,1.32	<0.01	1.24	1.19,1.30	<0.01	1.08	1.04,1.11	<0.01
Tumor grade			<0.01			<0.01			0.07
1,2	-			-			-		
3,4	2.79	1.61,4.82		1.83	1.25,2.69		1.21	0.99,1.47	
Histology			<0.01			<0.01			<0.01
Non-clear cell	-			-			-		
Clear cell	2.67	1.40,5.09		3.09	1.86,5.14		1.37	1.10-1.70	
Preoperative GFR (per 10 units)	1.04	0.90,1.19	0.60	0.95	0.85,1.07	0.42	0.86	0.81,0.92	<0.01
New-Baseline GFR (per 10 units)	1.02	0.86,1.20	0.83	0.97	0.84,1.11	0.67	0.96	0.89,1.03	0.26

* Tumor stage was also a significant factor but was not added to this model due to very strong collinearity with tumor size

Conclusion

- Our data confirm that CSM for RCC is primarily associated with aggressive tumor characteristics, and do not support oncologic protection related to greater preservation of renal function

- The relative indications for PN and RN remain unclear, particularly for tumors with increased oncologic potential and high tumor complexity. Prospective studies of PN vs. RN will be needed to provide higher quality data

Questions / comments:

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