

# Do we need to treat small renal masses in elderly patients?

인제의대 부산백병원

이 찬 호

# Definition and Characteristics of Small renal mass (SRM)?

## Definition of SRM

- **American Society of Clinical Oncology Clinical Guideline. 2017**
  - : incidentally detected
  - : contrast-enhancing solid or cystic lesion that is  $\leq 4\text{cm}$
  - : consistent with clinical stage **T1a RCC**
- **Most retro- & prospective studies**
  - : renal mass  $\leq 4\text{cm}$  (include **both malignant and benign masses**)

## **Pathologic characteristics of SRM** : (Mayo clinic, surgically treated)

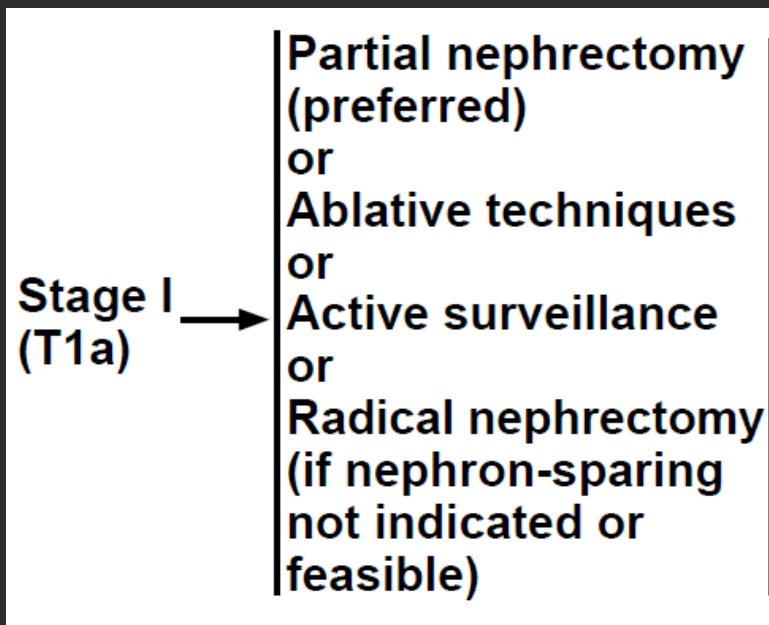
- 80% are malignant : most are low-grade, early stage tumors
- 20% are benign

# Current guidelines on SRM

## Localized 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

EAU guidelines on RCC, 2019



**Active surveillance is an option for the initial management of patients with clinical stage T1 renal lesions**

NCCN guidelines on Kidney Cancer, V1.2021

# Elderly Patients

- 65세 : 사회학적, 의학적 기준

- 고령 사회? 고령화 사회?

→ 총 인구 중 65세 이상의 인구가 차지하는 비율로 분류

고령화사회 (Ageing society) : 7% 이상

고령사회 (Aged society) : 14% 이상

초고령사회 (Post-aged society) : 20% 이상

# 노인 인구 증가 추이(65세 이상 기준, 단위: 만명, 괄호는 전체인구 중 비율(%))

[http://post.naver.com/pmg\\_books](http://post.naver.com/pmg_books)



시사상식사전 : 박문각

한국 : 2000년 (고령화 사회), **2017년 (고령사회)**, 2026년 (초고령사회 예상)  
\* 미국 : 2030년 (초고령사회 예상)

# Senior patients with SRM are more frequently referred for possible surgical resection!

- Surgery : Radical Nx. Partial Nx.
- Ablation : Radiofrequency ablation, Cryoablation

**Standard Treatment**

- Expectant management : Active surveillance or Watchful waiting
  - ⇒ Evidences against surgical treatment in elderly patients
    - **Oncologic outcomes**
    - **Complications after surgery**
    - **Competing risk to mortality or death**

## Evidences against surgical treatment in elderly patients

- **Oncologic outcomes**
- Complications after surgery
- Competing risk to mortality or death

Original Article

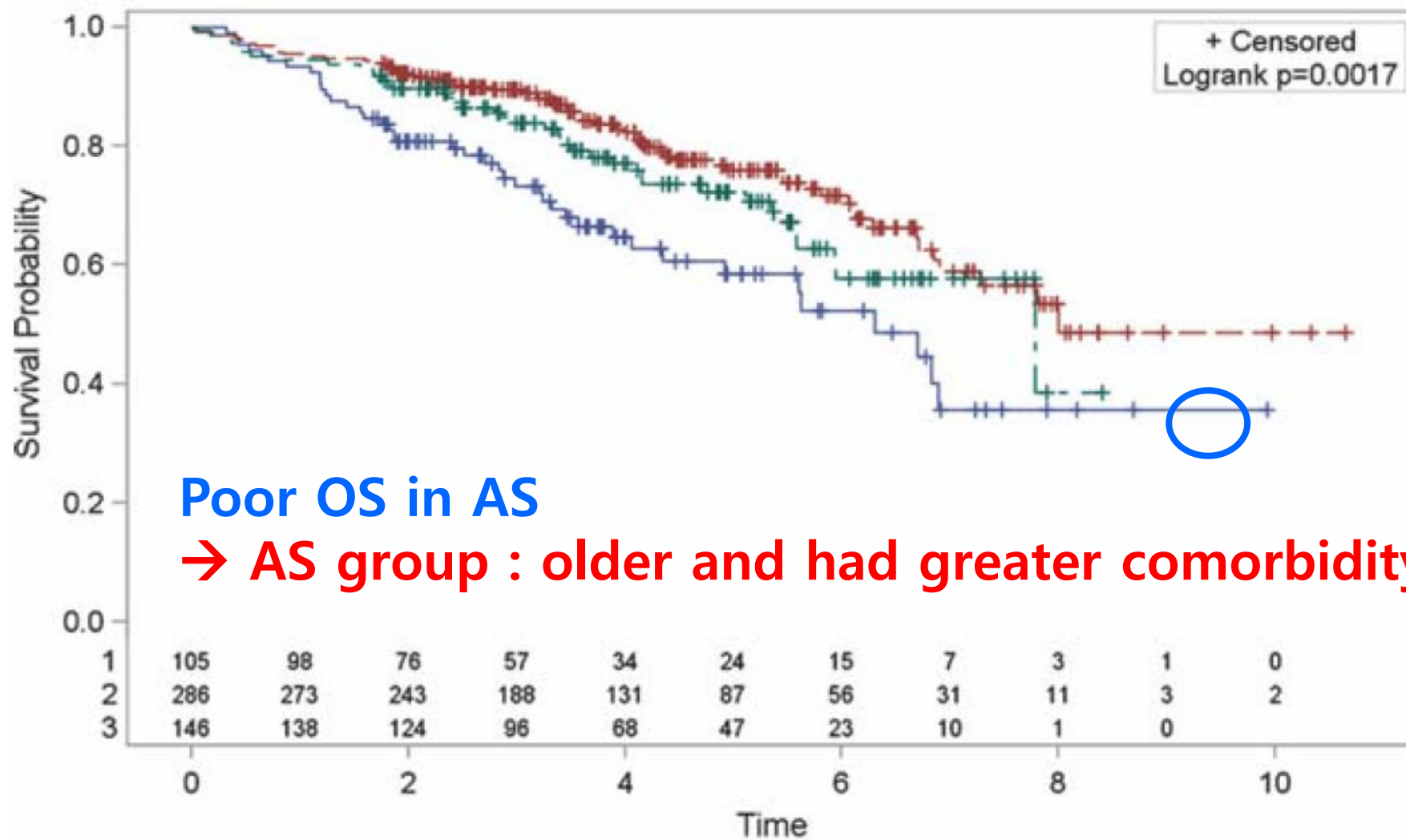
# Active Treatment of Localized Renal Tumors May Not Impact Overall Survival in Patients Aged 75 Years or Older

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

- Cleveland Clinic kidney cancer database
- 537 patients, retrospective study
- **T1 renal tumors ( $\leq 7\text{cm}$ ) detected at age  $\geq 75$  years**
  - : Surveillance (20%), Partial Nx. (53%), Radical Nx. (27%)
  - Survival according to treatment methods

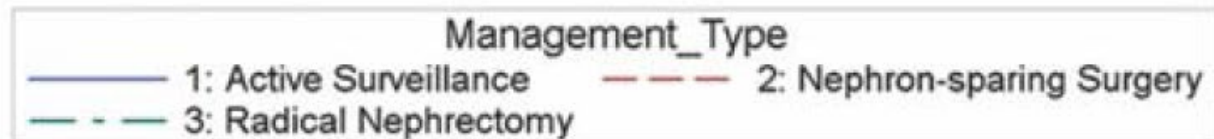


# Evidences against surgical treatment : **Oncologic outcome**



**Poor OS in AS**

**→ AS group : older and had greater comorbidity!**



# Evidences against surgical treatment : **Oncologic outcome**

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

Variable	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
<b>T1, age ≥75</b>				
<b>Management type</b>		.0021		.22 <sup>a</sup>
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
<b>Race</b>		.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/1.73m <sup>2</sup> decrease	1.11 (1.03-1.20)	.0079	1.02 (0.93-1.11)	.68

# Evidences against surgical treatment : **Oncologic outcome**

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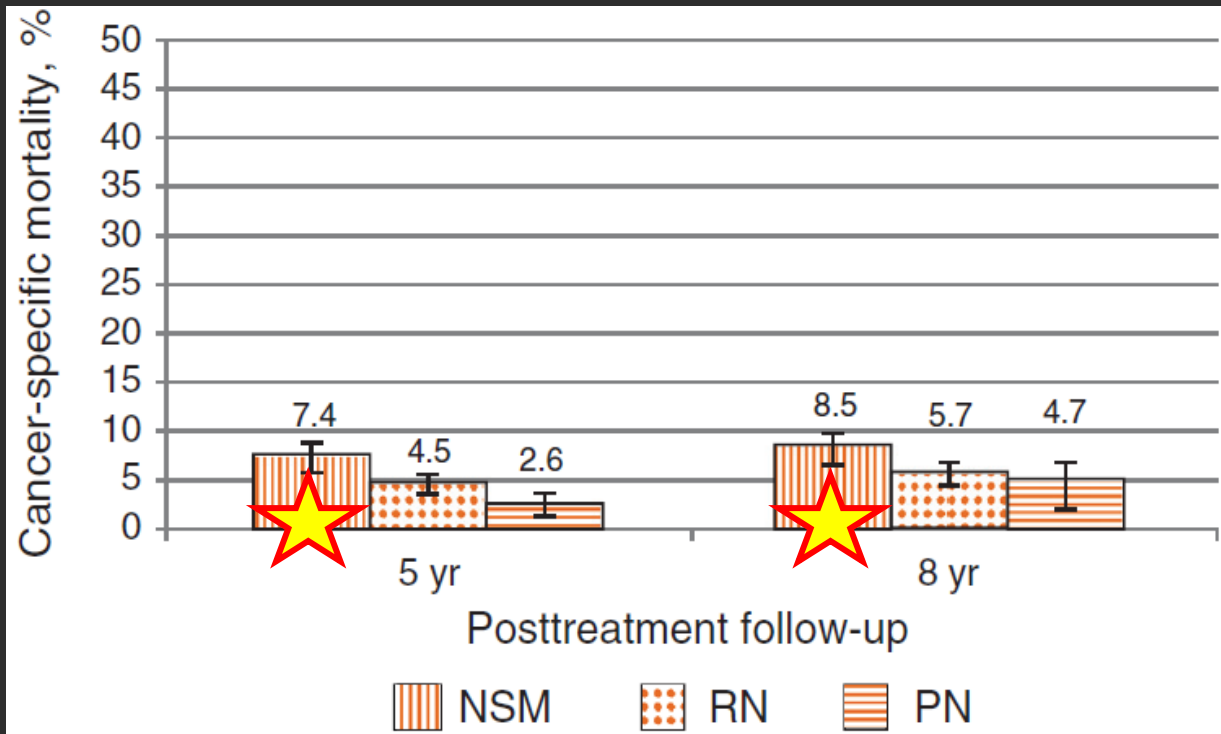
• The most common cause of death : Cardiovascular (29%)  
 : Cancer progression only 4% of deaths.  
 → Active treatment may not impact OS !

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

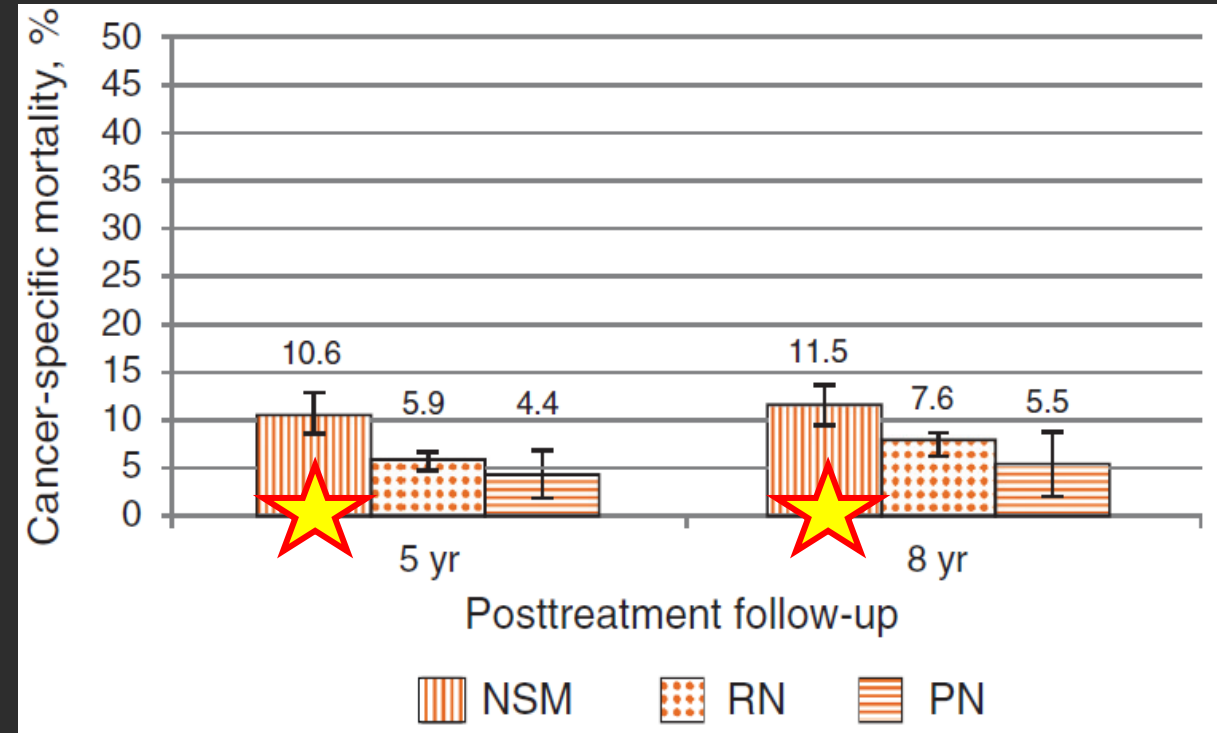
*Maxine Sun<sup>a,b,1,\*</sup>, Andreas Becker<sup>a,c,1</sup>, Zhe Tian<sup>a</sup>, Florian Roghmann<sup>a,d</sup>, Firas Abdollah<sup>a,e</sup>, Alexandre Larouche<sup>a</sup>, Pierre I. Karakiewicz<sup>a,f</sup>, Quoc-Dien Trinh<sup>a,f</sup>*

- Medicare beneficiaries, between 1988 and 2005
- 10595 patients, retrospective study
- **T1 RCC, aged  $\geq$  66years**
  - : Non-surgical management (31%), Partial Nx. (10%), Radical Nx. (59%)
  - Cancer-specific mortality according to treatment methods

## Cumulative incidence of cancer-specific mortality rates



T1a RCC, ≥66 yr



T1a RCC, ≥ 75yr

Non-surgical management : Worse Cancer Specific Mortality



## Multivariable competing risk regression analysis

	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
RCC only <sup>a</sup> , n = 7806	0.26 (0.13–0.54)	0.01	0.48 (0.27–0.85)	0.01

PN or RN : Reduction of CSM among older patients ( $\geq 66$ years)

No CSM difference in  $\geq 75$  years or  $\geq 75$  years with SRM

## Evidences against surgical treatment in elderly patients

- Oncologic outcomes
- **Complications after surgery**
- Competing risk to mortality or death

# Assessing the Burden of Complications After Surgery for Clinically Localized Kidney Cancer by Age and Comorbidity Status

Jeffrey J. Tomaszewski, Robert G. Uzzo, Alexander Kutikov, Katie Hrebinko, Reza Mehrazin, Anthony Corcoran, Serge Ginzburg, Rosalia Viterbo, David Y. T. Chen, Richard E. Greenberg, and Marc C. Smaldone

- Fox Chase Cancer Center, 1092 patients, retrospective study
- **Stage I ~ II renal tumor** : Partial (71.9%) & Radical (28.1%) Nx.
- **90-day Complications rate ?**
  - Low risk patients (CCI  $\leq$  2 or age  $\leq$  75 years) (23.4%)
  - High risk patients (CCI  $>$ 2 or age  $>$ 75 years) (76.6%)**



**Low risk (CCI  $\leq$  2 or age  $\leq$  75 yrs)**

**vs. High risk (CCI  $>$ 2 or age  $>$ 75 yrs)**

- 90-day complication : 14.1 % vs. **22.4%**
- No difference in complications according to treatment type  
(Partial vs. Radical)
- Multivariate analysis
  - **Elderly and comorbid patients with RCC**  
: twice as likely to experience a complication (**odd ratio 1.9 (CI : 1.3-2.8)**)

## Evidences against surgical treatment in elderly patients

- Oncologic outcomes
- Complications after surgery
- **Competing risk to mortality or death**

## Competing risks to mortality

SRM : Surgical resection or Ablation

→ **Survival benefit ?**

: in terms of **cancer specific survival**

→ **No Survival benefit ?**

: in terms of **overall survival** or **other cause of death**

- Life expectancy, Comorbidity (cardiovascular, other cancer...)

# Competing risks to mortality : SEER Population based

## Competing Risks of Death in Patients with Localized Renal Cell Carcinoma: A Comorbidity Based Model

Alexander Kutikov,\* Brian L. Egleston,\* Daniel Canter, Marc C. Smaldone, Yu-Ning Wong and Robert G. Uzzo†

*From the Department of Urological Oncology (AK, DC, MCS, RGU), Biostatistics (BLE) and Medical Oncology (YNW), Fox Chase Cancer Center, Temple University School of Medicine, Philadelphia, Pennsylvania*

1995-2005, 6,655 patients with localized RCC : SEER-Medicare data set

Patients

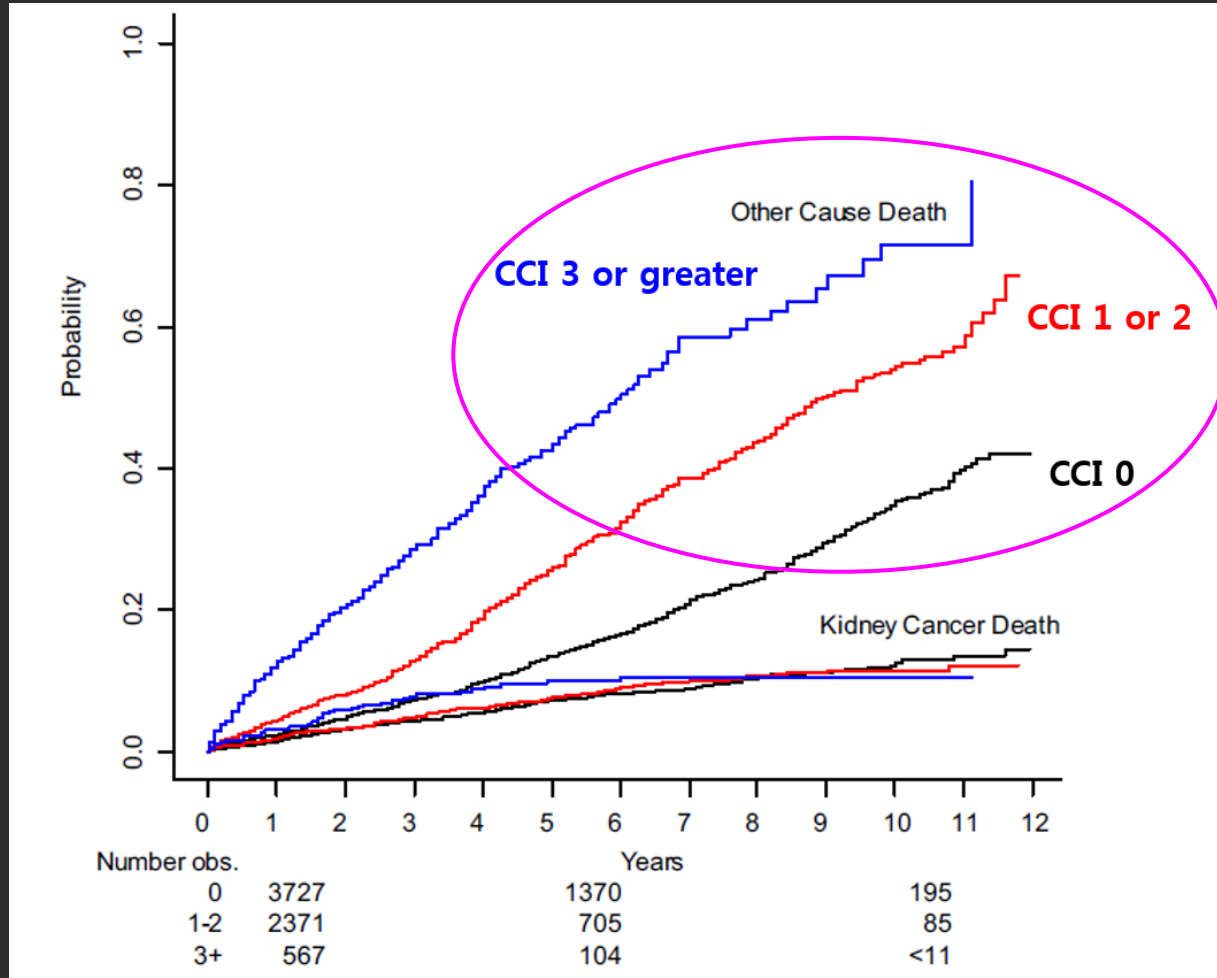
Older than **65yr** (median 73yr)

→ The impact of **kidney cancer** vs. **competing cause of death**

: 4 prognostic markers (race, gender, tumor size, age) + Charlson Comorbidity Index (CCI) score

# Competing risks to mortality : SEER Population based

Surgically treated localized RCC patients!



Cumulative incidence of death :

: **Other cause death** > kidney cancer Death

: **More comorbidity** > Without comorbidity

# Competing risks to mortality : Cardiovascular risk

## Balancing cardiovascular (CV) and cancer death among patients with small renal masses: modification by CV risk

Hiten D. Patel<sup>†‡§</sup>, Max Kates<sup>†</sup>, Phillip M. Pierorazio<sup>†</sup> and Mohamad E. Allaf<sup>†‡</sup>

<sup>†</sup>James Buchanan Brady Urological Institute, and <sup>‡</sup>Center for Surgical Trials and Outcomes Research, Department of Surgery, Johns Hopkins Medical Institutions, and <sup>§</sup>Epidemiology and Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

1995-2007, 7177 patients with localized RCC : SEER-Medicare data set

Patients

**Older than 65yr, T1a ( $\leq 4\text{cm}$ )**

Radical Nx. (63.7%), Partial Nx. (25.8%), **Deferred therapy (10.5%)**

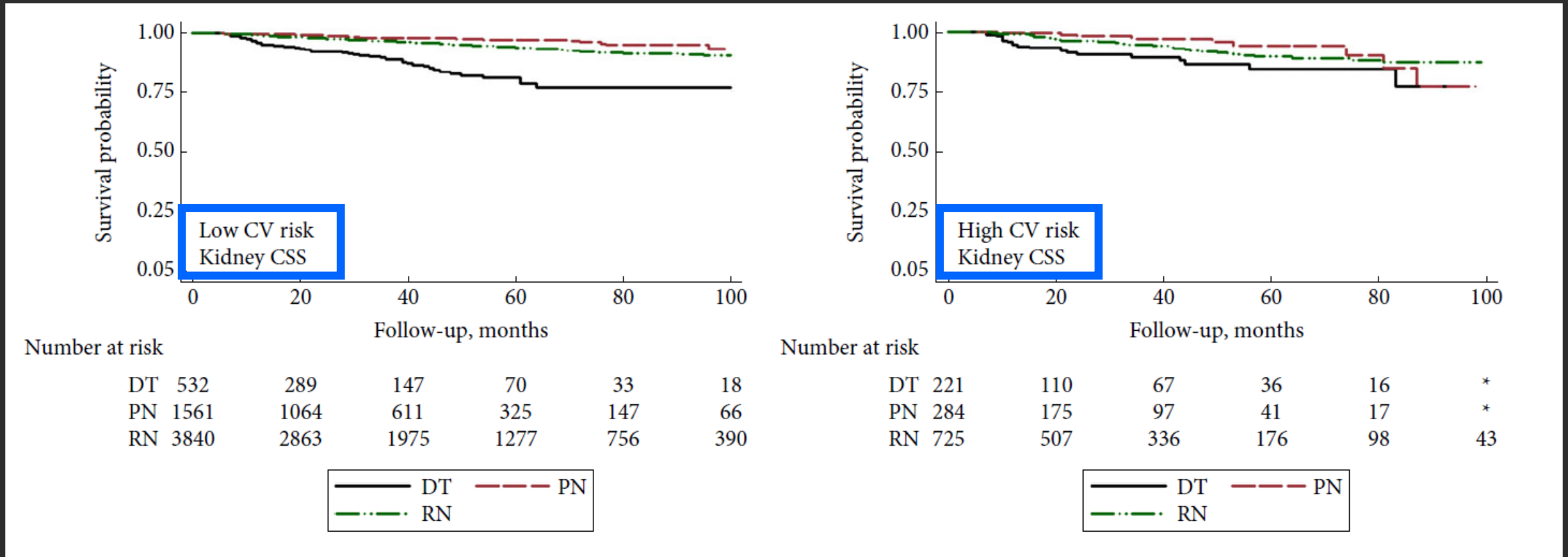
\* **DT : lacking of surgery within 6 months of diagnosis**

High CV risk : congestive heart failure, cerebrovascular dz, history of MI, peripheral vascular dz

Low CV risk : absence of any of these

# Competing risks to mortality : Cardiovascular risk

## CV risk modified CSS



Surgery was favored over DT for patients at low CV risk (Nx. vs DT, HR 0.33, 95%)

No statistically significant difference for patients at high CV risk!

## Evidences against surgical treatment in elderly patients

- : Expectant management (Active Surveillance or Watchful waiting)
  - could be one of the treatment options in selected elderly patients

### Results of AS in prospective studies

- Canadian (cT1N0M0) : LGR 0.13cm/yr, 1.1% mets, 12% progressed
- DISSRM (cT1N0M0) : LGR 0.09cm/yr, 0% mets, 14% delayed intervention
- Fox Chase (cT1-2N0M0) : LGR 0.19cm/yr, 1.8% mets, 34% delayed intervention

linear growth rate (LGR) : cm / year

### Limitations

Short median f/u periods!, Metastasis!, Delayed intervention!



**In a real clinical setting,  
how often have you performed  
expectant management in elderly patients?**

# Trends in RN, PN, Ablation, and Surveillance : Tumor size



## Evolving practice patterns for the management of small renal masses in the USA

Glen Yang, Jacqueline D. Villalta, Maxwell V. Meng and Jared M. Whitson

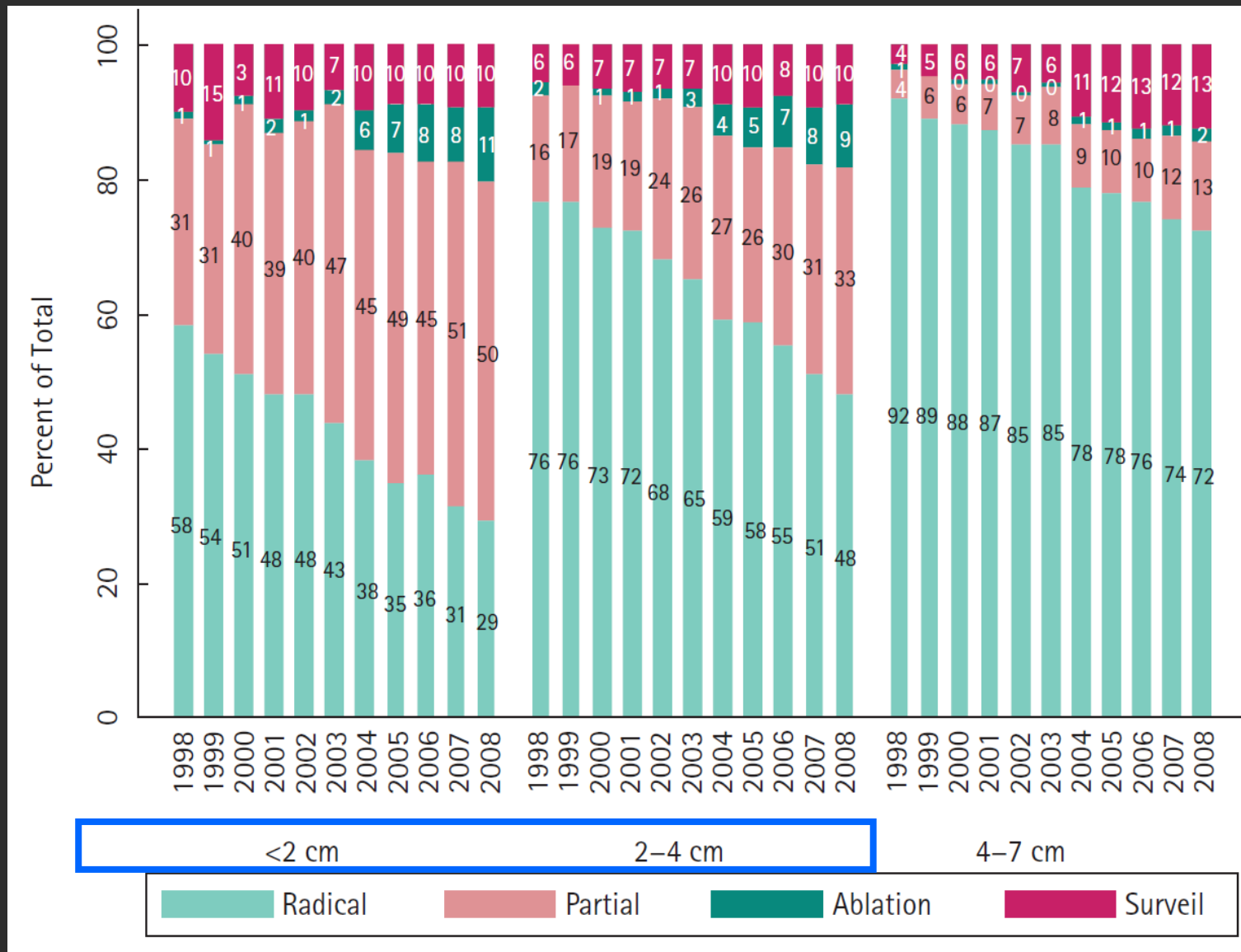
*Department of Urology and Helen Diller Family Comprehensive Cancer Center, University of California San Francisco, San Francisco, CA, USA*

Accepted for publication 9 November 2011

**Masses of  $\leq 7$  cm in the SEER database 1998 – 2008**

**48,148 Patients, mean age 63.4 yeras**

# Trends in RN, PN, Ablation, and Surveillance : Tumor size



# Trends in RN, PN, Ablation, and Surveillance : Age

Characteristic	<u>RN</u> <i>N</i> (%)	<u>PN</u> <i>N</i> (%)	<u>Ablation</u> <i>N</i> (%)	<u>Surveillance</u> <i>N</i> (%)	<u>Total</u> <i>N</i> (%)
Age, years:					
<50	5 023 (16.4)	1 773 (15.6)	282 (16.4)	684 (15.5)	7 762 (16.1)
50–59	6 838 (22.3)	2 644 (23.2)	399 (23.2)	1 006 (22.7)	10 887 (22.6)
60–69	8 066 (26.3)	3 014 (26.5)	439 (25.6)	1 124 (25.4)	12 643 (26.3)
70–79	6 964 (22.7)	2 573 (22.6)	379 (22.1)	1 067 (24.1)	10 983 (22.8)
>80	3 734 (12.3)	1 374 (12.1)	219 (12.7)	545 (12.3)	5 872 (12.2)

# Reasons not to perform Expectant management in SRM?

In a real clinical setting....

- No severe surgical complications.
- Widespread of Minimally invasive surgery.
- Lack of adequate tools for selecting patients.

# Selecting patients for AS or intervention : Guidelines

Guideline	Criteria for AS
ASCO, 2017 <sup>3</sup>	Absolute indications: high risk for anesthesia or life expectancy < 5 years Relative indications: significant risk of ESRD if treated, SRM (< 1 cm), or life expectancy < 10 years Initial management option for patients who have significant

## Calculator or Indicator or Monogram?

	intervention
EAU, 2015 <sup>23</sup>	Elderly and/or comorbid patients with SRM and decreased life expectancy AML

# Nomogram : Quantitate competing causes of mortality

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

## 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

J Clin Oncol. 2010 28(2):311-317

## Competing Risks of Death in Patients with Localized Renal Cell Carcinoma: A Comorbidity Based Model

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J Urol. 2012 188(6):2077-2083

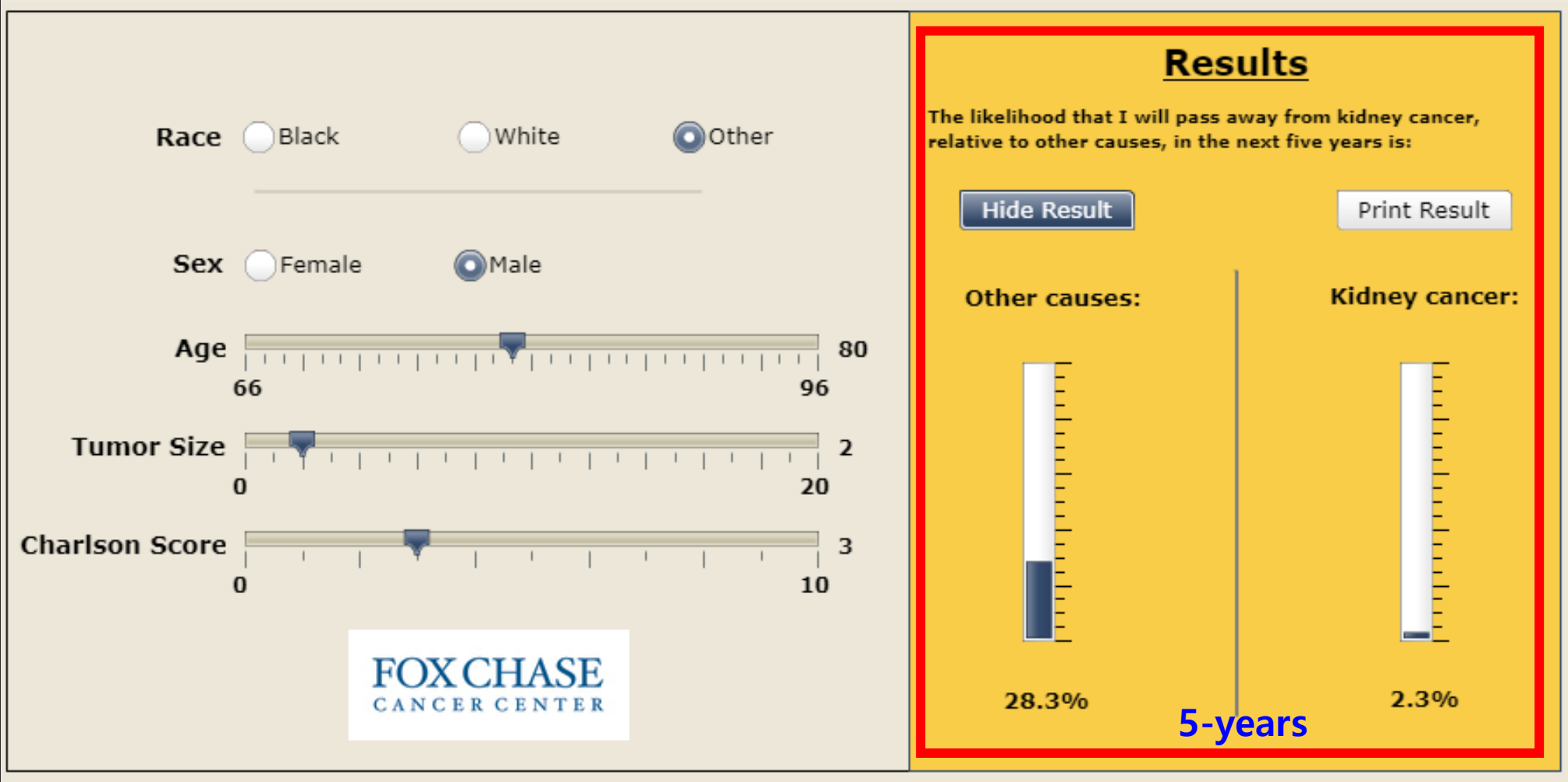
1998-2003, 30,801 patients with localized RCC (cancer-directed surgery +) : SEER data base  
1995-2005, 6,655 patients with localized RCC : SEER-Medicare data set

4 prognostic markers (race, gender, tumor size, age) + Charlson Comorbidity Index (CCI) score

→ Nomogram : Quantitate competing causes of mortality

**Fox Chase cancer center : [labs.fccc.edu/nomograms](http://labs.fccc.edu/nomograms)**

# Korean, Male, 80yr, 2cm, CCI 3





# Selecting patients with SRM for **AS** or **Intervention**

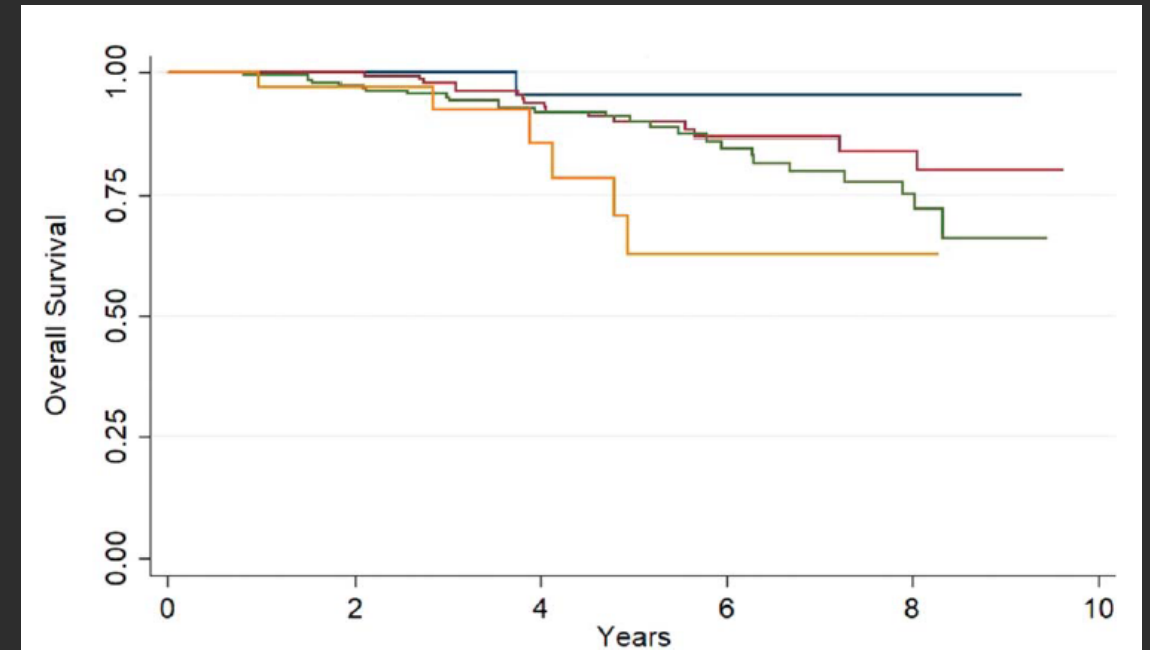
## DISSRM Score formula table

Points	0	1	2	
Age	<60	60-70	>70	-
CCI	0	1	≥2	-
Tumor Diameter	< 2 cm	2-3 cm	> 3 cm	-
PCS	≤ 45	> 45	-	-
				*Sum = DISSRM Score

Total Score ranging from 0 to 7

CCI : Charlson comorbidity index

PCS (Physical Component score) : SF-12



**Figure 3.** Kaplan-Meier curve of overall survival stratified by DISSRM Score. Curves represent scores of 0 or 1 (blue), 2 or 3 (red), 4 or 5 (green) and 6 or 7 (yellow).

**Higher DISSRM score → Worse OS, Candidate for AS**

# Conclusion : SRM in elderly patients : Treat? or Not Treat?

- Elderly patients with incidental SRM have a **low RCC-specific mortality** and **significant competing-cause mortality**.
- **SRM with low comorbidity**
  - Initial intervention → **Excision or Ablation** : Standard of care
  - Initial AS ± **Delayed intervention** → Could be possible  
(Canadian, DISSRM, Fox Chase)  
Delayed intervention : linear growth rate  $\geq 0.5\text{cm/year}$
- **SRM with high comorbidity**
  - **Competing risk** : Expectant management or Excision or Ablation