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Surveillance of renal masses – are we ready?

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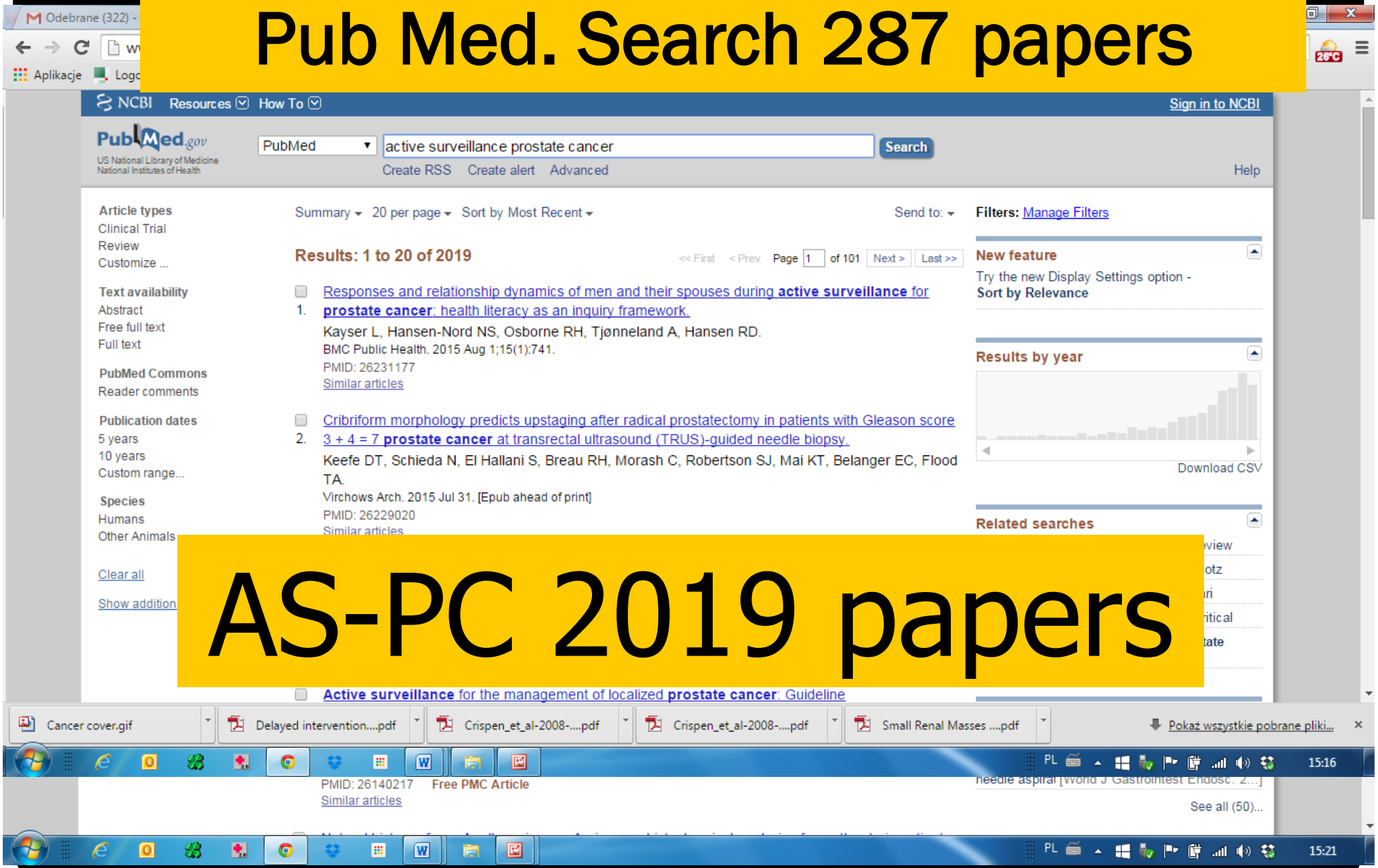
Pub Med. Search 287 papers



AS-PC 2019 papers

143 000 new cases of RCC were diagnosed in 2012

Ferlay J at all, 2012

Small renal mass (SRM)

- Solid tumor < 4 cm enhancing on CT and MRI and suspected of being RCC

  Gill IS at all, NEJM 2010

- 20% SRM show aggressive potential
- 20% benign lesions
- 60% indolent biological potential

  Lane BR et al. J. Urol. 2007
  Remzi M. et al. J. Urol. 2006
  Frank I et al. J. Urol. 2003

- 79%-84% SRM detected before genitourinary symptoms are present

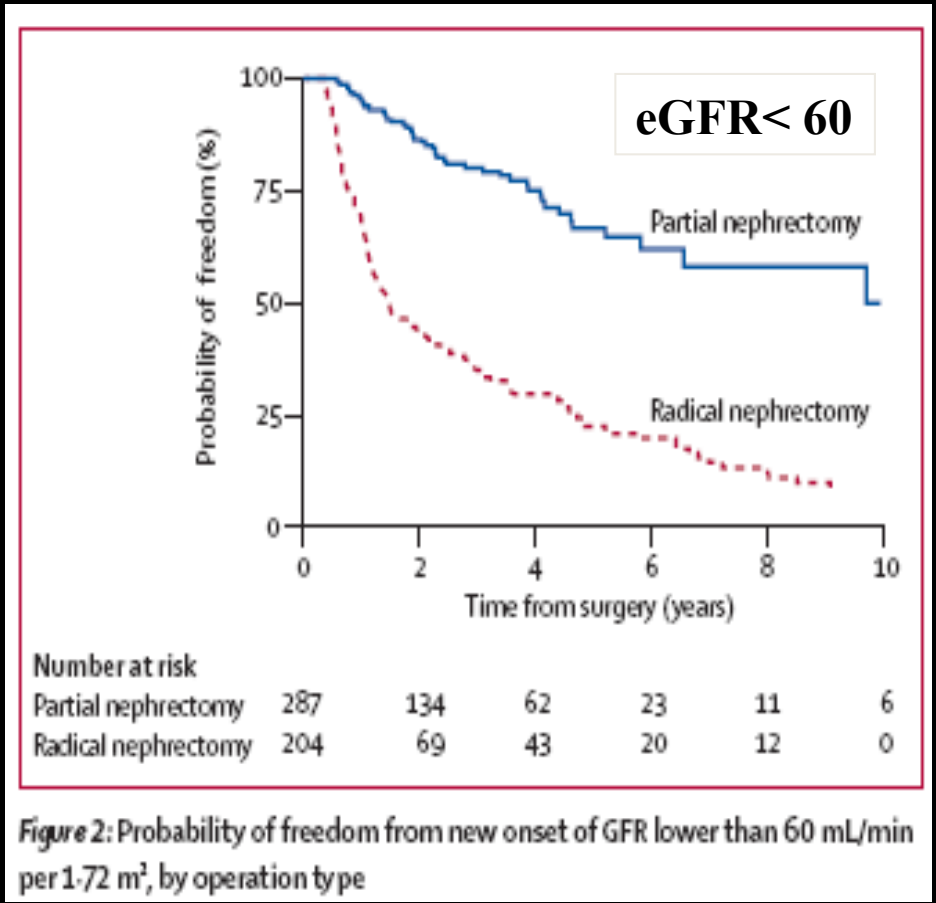
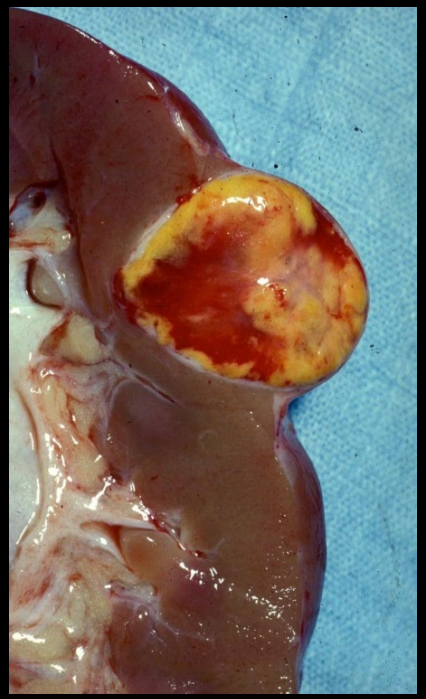


Figure 2: Probability of freedom from new onset of GFR lower than 60 mL/min per 1·72 m², by operation type



Nefrectomy should be avoided

EAU guidelines –recomendations for AS

Conclusions	LE
Population-based analyses show a significantly lower cancer-specific mortality for patients treated with surgery compared to non-surgical management. However, the same benefit in cancer-specific mortality is not confirmed in analyses focusing on older patients (> 75 years old).	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
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

Recommendations	GR
Due to the low quality of the available data no recommendation can be made on radiofrequency ablation and cryoablation.	C
In the elderly and/or comorbid patients with small renal masses and limited life expectancy, active surveillance, radiofrequency ablation and cryoablation can be offered.	C

RCC can be cured only when the tumor is organ-confined, and surgery is the only curable treatment modality

(at least in 2015)

Active surveilance

Prostate Cancer v. Renal Tumors

PC	Renal Tumor
Markers (PSA, PCA3)	No markers
mpMRI	CT, MRI but … GFR
Biopsy - easy	Biopsy difficult
QL (ED, Incontinence)	QL ?

ies

In SRMs mean size difference between CT and pathological specimen not significant.
In all RMs CT overestimates ccRCC size and underestimates papillary RCC size
No statistical difference between CT and pathological size in all RMs or SRMs
Sensitivity 70–75 % in predicting papillary-RCC

Accuracy 90 % in differentiating ccRCC and Oncocytoma

PPV 43 %, NPV 84 %, sensitivity 60 %, specificity 73 % in predicting benign tumour

Area under ROC curve arterial phase 0.860, venous phase 0.711 and delayed phase 0.571 in distinguishing Oncocytoma from RCC
Diagnostic accuracy in distinguishing AML from ccRCC 0.59 in all RMs.
Low SI index in T2-wighted images combined with< 2 cm size accuracy of 98 %
Sensitivity 100 %, specificity 100 % in differentiating ccRCC from non-ccRCC, AML or Oncocytoma
Sensitivity 86 %, specificity 88 % in differentiating AML from Oncocytoma
PPV 94.4 %, NPV 69.4 %, sensitivity 86.2 % and specificity 85.9 % in differentiating ccRCC in all tumour sizes
Sensitivity 82.8 % in differentiating ccRCC in SRMs
Accuracy 78 % in differentiating RCC from angiomylipoma, oncocytoma and pseudotumours

Author Year (ref.)	Total cohort (n) / Sub-cohort SRMs (n)	Ind test		Level of evidence
Kurta et al. 2009 [24•]	521/263	CT	e between CT and significant. ccRCC size and CC size	2b
Lee et al. 2010 [25]	467/239	CT	een CT and pathological	2b
Pierorazio et al. 2013 [31•]	100 /100	CT	cting papillary-RCC	2b
Gakis et al. 2010 [32]	20/ 20	CT	ting ccRCC and Oncocytoma	3b
Millet et al. 2011 [34•]	99/99	CT,	itivity 60 %, specificity tumour	1b
Bird et al. 2011 [35•]	79/79	CT	al phase 0.860, venous phase .571 in distinguishing	3b
Hindman et al. 2012 [42]	108/40 <3 cm	MI	guishing AML from ccRCC	2b
Agnello et al. 2013 [43]	47/47	MI	images combined with< % 100 % in differentiating AML or Oncocytoma 88 % in differentiating	3b
Divgi et al. 2013 [51•]	195/101	PE	ensitivity 86.2 % and entiating ccRCC in all	2b
Jinzaki et al. 1998 [53]	64/64	US	tiating ccRCC in SRMs ting RCC from na and pseudotumours	3b

Imaging

- **PET CT with radioactively labelled antibody 1241 –girentuximab**
- **Tumor size sensitivity 86%, specificity 86% versus 76% and 47% for conventional CT**
- **For SRM sensitivity 82,8**

Divigy et all: J Clin Oncol. 2013

Limitations for contrast enhanced imaging – impaired renal function very often present in older patients suitable for AS

Biopsy or not to biopsy in AS?

- Non diagnostic rate for percutaneus renal biopsy (PRB) is aproximately 20%

  Leveridge et all; Eur. Urol. 2011, Menogue et all: BJIU Int. 2013

- Ability to distinguish high and low grade tumors aprox. 50%

  Ball et all: J. Urol 2015

- Old cormobid patient is suitable for AS (at least initially) regardless of PRB result
- For young patient PRB (with low rate of accuracy or NSS at the very beginning?

What do we know about AS?

Table 1 Mc dant, retrospective and prospective series repc illance for cT1a renal tum

Author	Patients/tumors (*n*)	Mean age (years)	Mean tumor size (cm)	Mean tumor growth rate (cm/year)	Mean follow up (months)	Delayed surgery, *n* (%)	Progres to meta *n* (%)	Deaths, *n* (%)
Chawla *et al*	61	–	2.97	0.20	36.0	20 (32.8%)	1.6%	0 (0%)
Volpe *et al.*[1	29/32	71	2.48	0.10	38.9	8 (27.5%)	0%	2‡ (6.9%)
Abou Youssi	35/44	78.1	2.2	0.21	47.6	8 (22.9%)	5.7%	9‡ (25.7%)
Mason *et al.*	82/84	74	2.6	0.25	36.0	12 (14.6%)	1.2%	7‡ (8.6%)
Brunocilla *et*	62/64	75	2.0	0.40	91.5	16 (25.8%)	3.2%	1§ (1.2%)
Crispen *et al*		69	2.45	0.29		68 (39%)	1.3%	18‡ (29%)
Rosales *et al*	154/173	71	2.8	0.34	31	11 (5%)	1.9%	2§ (3.2%)
Abouassaly	212/223	81	2.5	0.24	35	4 (3.6%)	0%	0 (0%)
†Jewett *et a*		73	2.1	0.13		9 (5%)	1.1%	14‡ (6.6%)
Haramis *et a*	110/110	71.7	2.67	0.15	24	2 (4.5%)	0%	1§ (0.5%)
Repetitive cc	178/209	d. †Prospective, Phase II study. ‡Non-cancer re			28		ated deaths.	34‡ (31%)
	44/51				77.1			10‡ (5.6%)
								2§ (1.1%)
								1‡ (2.2%)

Borghesi et all 2015

Metastatic progression - reviev

- **967 pts. – metastatic progression 0 - 5,7%**

Borghesi et all 2015

- **880 pts. – 18 pts. (2,04%) metastic (FU 40 months)**
- Metatstatic patients had
  - Larger tumors (4,1 +/- 2,1 cm vs. 2,3 +/- 1,3) p< 0,001
  - Faster growth rate (0,8 vs. 0,3 cm/year) p< 0,001

Smaldone et all: Cancer 2012

What about cT1b – cT2 renal tumors?

Author	Patients/tumors (*n*)	Mean age (years)	Mean tumor size (cm)	Mean tumor growth rate (cm/year)	Tumor biopsies, *n* (%)	Mean follow up (months)	Delayed surgery, *n*, (%)	Progression to metastases, *n* (%)	Deaths, *n* (%)
Lamb *et al.*[46]	36/36	76.1	6.0	–	–	24	0 (0%)	1 (2.7%)	13†
Mues *et al.*[23]	36/42	73.8	7.13	0.57	12 (33%)	36	5 (13.8%)	2 (5.6%)	4†
Mehrazin *et al.*[47]	68/72	68.9	5.3	0.44	21 (31%)	38.9	23 (34%)	0	9†

†Non-cancer related deaths.

Borghesi et all 2015

Angiomyolipoma (AML) – aprox. 3% of renal masses

- No randomized studies on AS vs. Surgery !!!!!
- Several retrospective papers, small numbers of patients
- Optimal size treshold for surgical intervention is still debated

  Nelson et all: J. Urol. 2002
- Risk factors for intervention: retroperitoneal and upper urinary tract bleeding (may be life threatening)

  Ramon et all: Eur. Urol. 2009,

  Zhang et all: J. Urol. 2002

- In Tuberous Sclerosis (TC) - Bourneville'a-Pringle disease - is more often multifocal, bilateral, larger and more likely to result in bleeding
- Presence of AML in lymph nodes is not meatstatic disease (multicentric genesis) and is also connected with TC
- AML can involve renal vein and even vena cava

Predictors for active treatment

- 130 pts, 53,3 years old +/- 16,5 years
- 70% < 4 cm
- 78% female

Tumor size > 4 cm and symptomatic presentation were clinical predictors at the multivariate analysis

- 17 pts (13%) underwent delayed surgical intervention

Ouzaid et all: BJU Int. 2014

Predictive factors of renal tumor aggressivenes and growth rates

- **Symptomatic tumors – yes**
- **Sex – conflicting data**
- **RENAL score – yes**
- **Size – conflicting data**

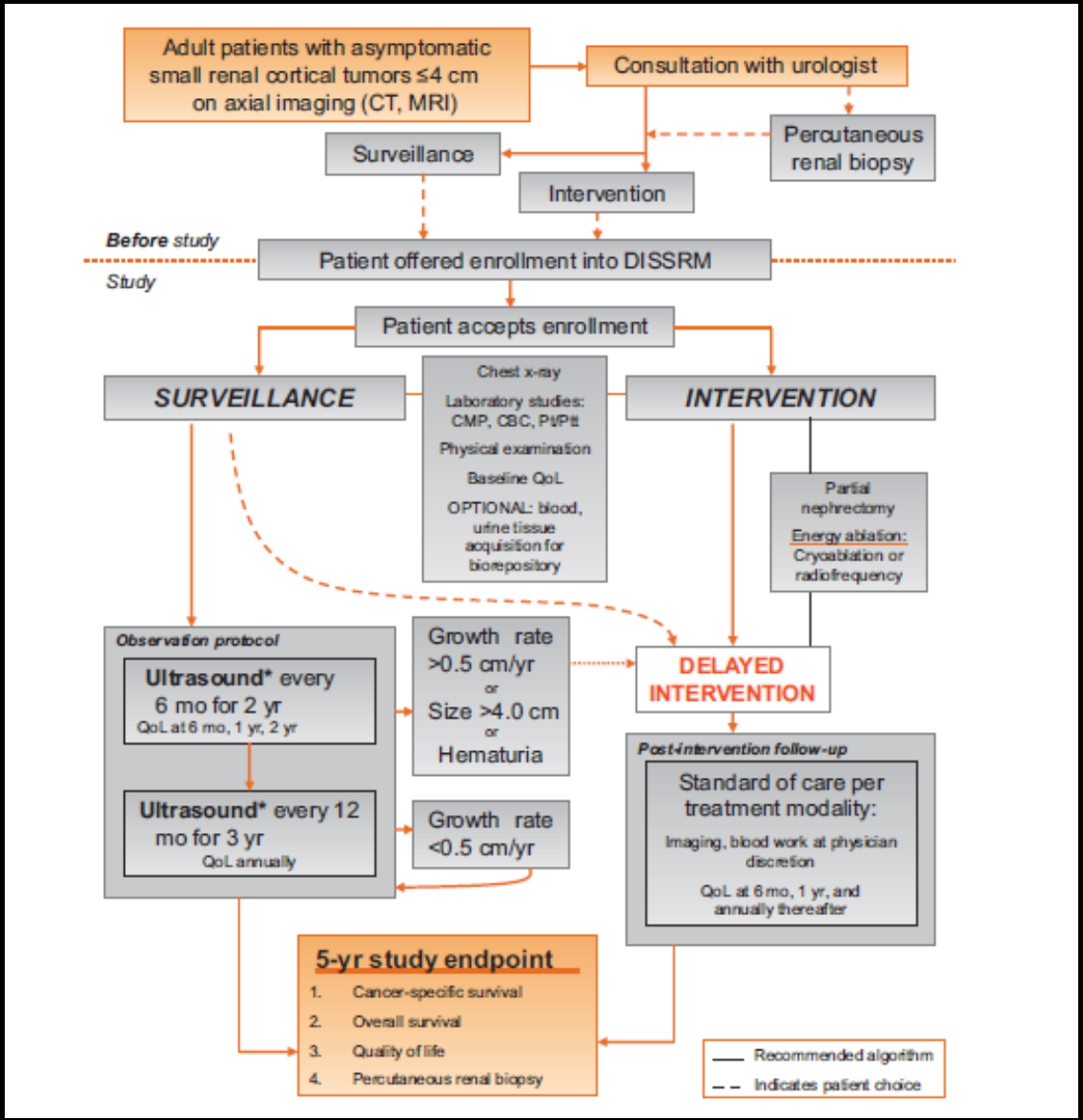
Schiavina R et all.: Clin. Genitourin. Cancer 2014

Matsumoto et all.: Int. J. Urol. 2014

Organ et all.: Can. Urol. Ass. J. 2014

Mason et all.: Eur. Urol. 2011

AS – how to do it?



Pierorazio et all: Eur. Urol. 2015

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]*

- **497 patients (non randomised – pts. choice)**
- **274 (55%) chose PI, 223 (45%) AS. 21 (9%) crossed over to delayed intervention**
- **2 years OS for PI 98% for AS 96%**
- **5 years OS for PI 92%, for AS 75%**
- **5 years CSS for PI 99%, for AS 100%**

(AS patients vere older , worse ECOG score, more comorbidities, smaller tumors but more often multiple or bilateral lesions)

Are we ready?

- Not yet
- We need to improve:
  - Imaging
  - Biopsy technique
  - Find predictive factors
  - Define schedule

Table 8.1: Definitions of active surveillance and watchful waiting (9-11)

	Active surveillance	Watchful waiting
Treatment intent	Curative	Palliative
Follow-up	Predefined schedule	Patient-specific

Conclusions

- AS is a valid first line option for patients with asymptomatic small AML
- AS may be offered to patients with incidental cT1a tumors who have relevant comorbidities. (low risk of metastatic progression and cancer specific mortality is reported in published papers)
- AS with delayed intervention seems to be noninferior management strategy for well selected patients with SRM
- For cT1b-cT2 renal masses as there is no strong evidence or proof of safety AS can be offered only for very motivated, well informed higly selected patients