

Renal cell carcinoma

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Clinical scenario I

Male 62 y.o.

- ✓ I did an ultrasound examination during a company check-up.
- ✓ They found **a mass in my kidney**.
- ✓ The exam describes it as **anechoic** and with a diameter of 4 cm.
- ✓ Help me! I have a kidney cancer. I need surgery right now!

Clinical scenario II

Male 62 y.o.

- ✓ I saw blood in the urine (**macroscopic haematuria**)
- ✓ I took an antibiotic and it is gone.
- ✓ Nothing to be worried about , isn't it?

Clinical scenario III

Male 62 y.o.

- ✓ I did an ultrasound examination during a company check-up.
- ✓ They found a **mass in my kidney**.
- ✓ The radiologist describes it as 4 cm in diameter. He told me that it is not a cyst, and recommended an urological consultation to arrange a **biopsy**.
- ✓ Let's do this biopsy right now!

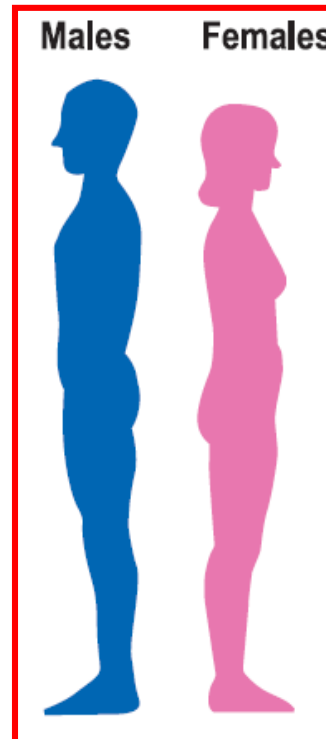
Clinical scenario IV

Male 62 y.o.

- ✓ I did an ultrasound examination during a company check-up
- ✓ They found a mass in my kidney
- ✓ The radiologist describes it as 4 cm in diameter. I had a CT scan that confirms it is a renal tumor.
- ✓ Doctor. I you to organize as soon as possible the removal of the entire kidney (**nephrectomy**).

Cancer Statistics: Incidence

1. Prostate 28%
2. Lung 15%
3. Colon 9%
4. Bladder 7%
5. Melanoma 5%
6. Kidney 4%



1. Breast 28%
2. Lung 14%
3. Colon 9%
4. Uterus 7%
5. Thyroid 5%
6. NH-Lymphoma 4%
7. Kidney 3%

Epidemiology

Renal cell carcinoma (RCC) represents 3-4% of all cancers but the diagnosis of a "renal mass (to be determined)" is very very frequent!

Age-standardised rate incidence of 5.8 and mortality of 1.4 per 100,000, respectively, in more developed areas



Population: 739.200,000

- Estimated new kidney cancer cases: 88,400
- Estimated deaths from kidney cancer: 39,300

- Annual increase of about 2% in the incidence
- Overall mortality rates for RCC increased up until the early 1990s, with rates generally stabilising in the following years, but increasing again in recent years

Siegel et al. CA Cancer J Clin 2012; 62: 10–29
European Association Urology guidelines 2015

Epidemiology

- **Renal cell carcinoma** is the commonest **solid lesion** in the kidney (approximately 90% of all kidney malignancies)
- It includes **different histological subtypes**, with specific histopathological and genetic characteristics
- There is a 3 : 2 predominance of men over women
- Age peak incidence between the **60 and 70 yrs**

Aetiology

- **Sporadic** renal carcinoma
- **Familial** renal carcinoma
(3-5% of all renal cancer)
- Renal carcinoma associated to **genetic syndromes**

Aetiology

Sporadic renal carcinoma

- ✓ Lifestyle habits such as smoking, obesity, and hypertension
- ✓ Smoking: increased relative risk in moderate-intermediate to heavy smokers (*La Vecchia et al. - Cancer Res. , 1990*)
- ✓ No direct relationship to exposure to industrial carcinogens

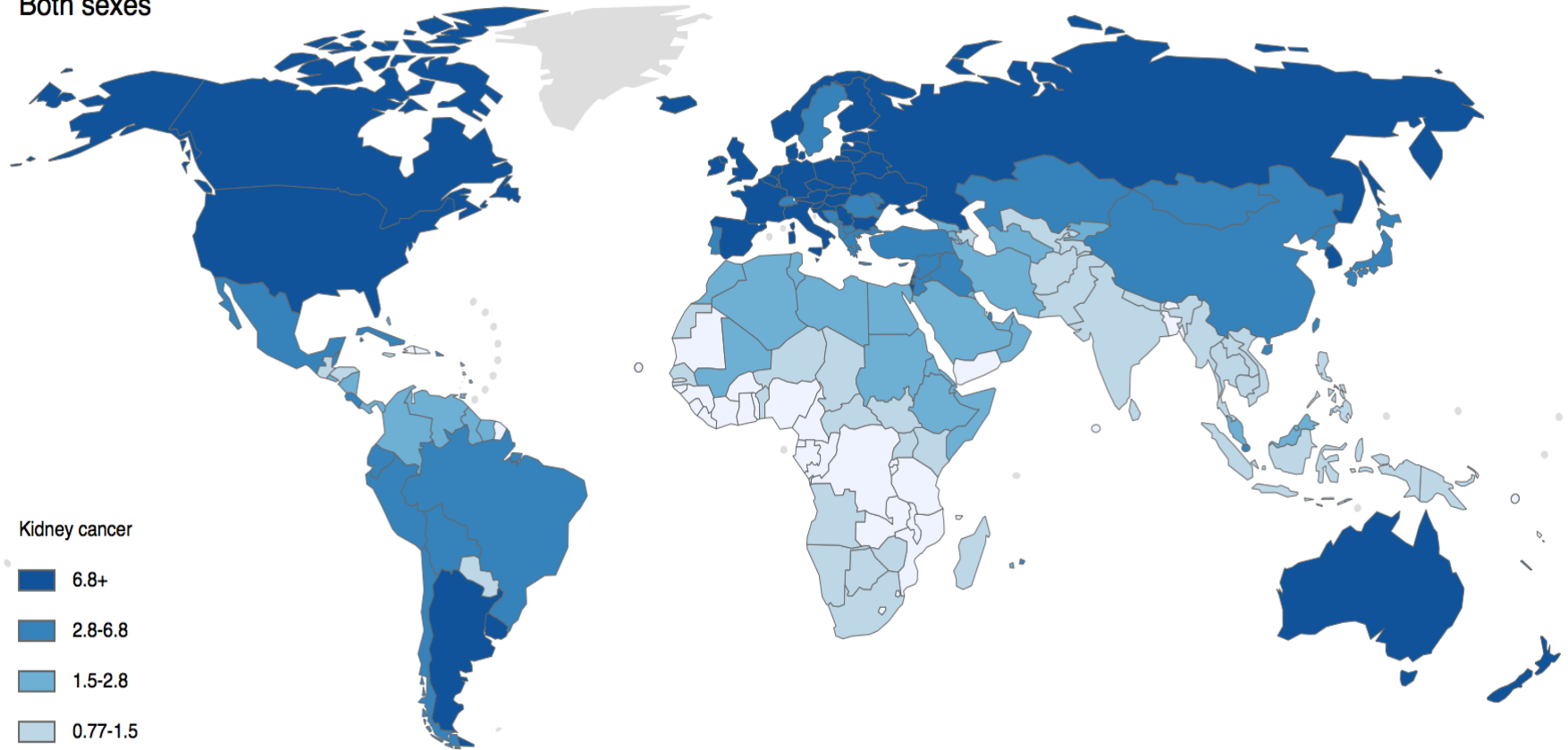
Recommendation	Strength rating
Increase physical activity, eliminate cigarette smoking and in obese patients reduce weight as the primary preventative measures to decrease risk of RCC.	Strong

Epidemiology

Geographical Distribution

Incidence ASR

Both sexes



Kidney cancer



International Agency for Research on Cancer



Source: GLOBOCAN 2012 (IARC)

Capitania U. and Montorsi F. The Lancet 2016

Aetiology

Sporadic Renal Carcinoma

- ✓ Loss of a segment of chromosome 3 is an **frequent occurrence** in patients with sporadic renal carcinoma
- ✓ Main **chromosomal alterations** observed in renal carcinoma: **deletions and translocations of the short arm of chromosome 3 (3p)**

Aetiology

Familial renal carcinoma

3-5% of all Renal Cancers

- ✓ Families with repeated cases of renal cancer, usually clear cell renal carcinoma, in which no gene mutations are evident and for which the gene responsible is not yet known.
- ✓ In a smaller proportion of these families a chromosomal translocation between chromosome 3 and another chromosome (the most frequent is translocation 3;8) has been observed.

Aetiology

Renal carcinoma associated with genetic syndromes

Von Hippel Lindau syndrome (1/36.000 births)

A rare familial condition with neoplastic predisposition.

- ✓ Hemangioblastomas of the retina, cerebellum and spinal cord, pheochromocytoma
 - ✓ Multiple renal tumors in different locations

Renal tumors: 35-45% of causes of death

Aetiology

Renal carcinoma associated with genetic syndromes

Recently identified the **suppressor oncogene**
VHL (Von Hippel Lindau) (3p 25-26).

Probably a gene therapy soon available?

Aetiology

Renal carcinoma associated with genetic syndromes

Hereditary Renal Papillary Carcinoma Syndrome (HRPC)

Characterized by the predisposition to develop **papillary type 1 renal carcinoma**

Papillary carcinoma is an infrequent renal tumor, accounting for 10-15% of renal neoplasm, and may be sporadic (one affected subject in the family) or **familial**.

RENAL MASSES: CLASSIFICATION

BENIGN

- Renal cyst
- Oncocytoma
- Angiomyolipoma

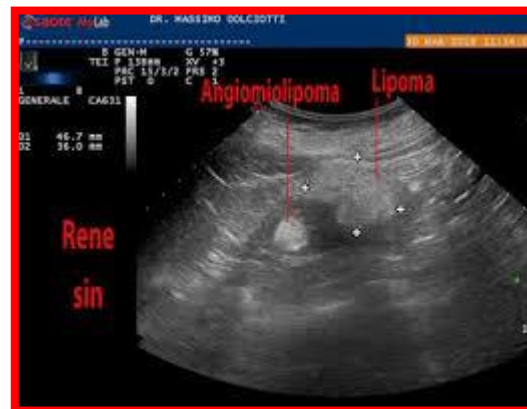
MALIGNANT

- Renal cell carcinoma
 - ✓ Clear Cell
 - ✓ Papillary I and II
 - ✓ Chromophobe
- Upper Tract Transitional Cancer
- Sarcoma
- Wilms Tumor

Most frequently diagnosed renal mass: renal cysts
benign or malignant ?

Clinical scenario

Incidental ultrasound detection of a renal mass



Renal cysts

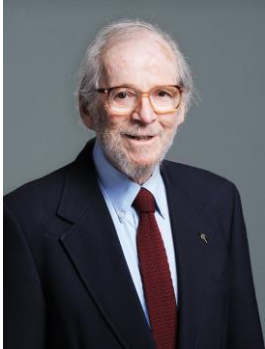


US anechoic lesions

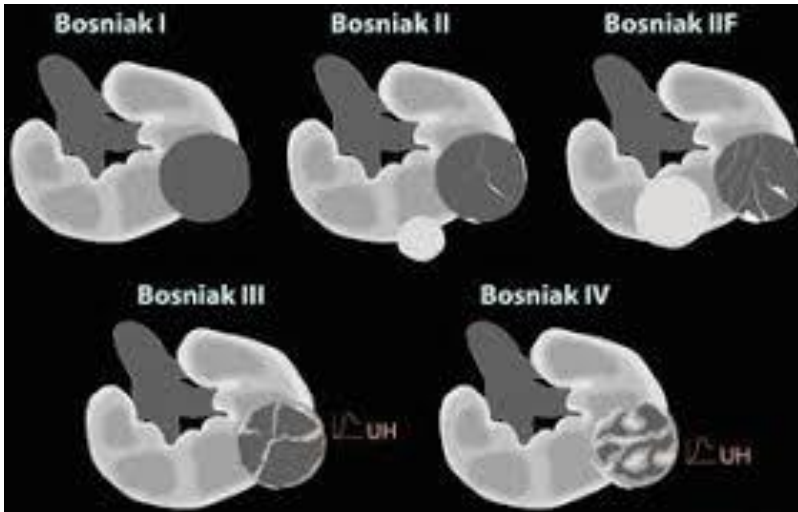
- ✓ Very frequent
- ✓ Always asymptomatic
(rarely heaviness sensation)
- ✓ Single or multiple

Always benign?

Renal cysts



Dr. Morton Bosniak



Bosniak Renal Cyst Classification System

- I** - **Simple cyst** with a hairline-thin wall.
 - No septa, calcifications, or solid components.
 - Water attenuation, no enhancement.

- II** - **Septa**: few hairline-thin in which not measurable enhancement may be appreciated.
 - **Calcification**: fine or a short segment of slightly thickened may be present in the wall or septa.
 - **High-attenuation**: uniform in lesions (< 3cm) that are sharply margined and do not enhance.

- IIF** - **Septa**: multiple hairline-thin in which not measurable enhancement of septum or wall is appreciated.
 - **Minimal thickening of wall or septa**, which may contain calcification, that may be thick and nodular, but no measurable contrast enhancement.
 - No enhancing soft-tissue components.
 - **Intrarenal**: totally intrarenal nonenhancing high-attenuating renal lesions; these lesions are generally well margined.

- III** - **Measurable enhancement**
Cystic mass with thickened irregular or smooth walls or septa in which measurable enhancement is present

- IV** - **Enhancing soft-tissue components**
Clearly malignant cystic masses that can have all of the criteria of category III but also contain distinct enhancing soft-tissue components independent of the wall or septa

Renal cysts

BOSNIAK CLASSIFICATION

Reference	Bosniak cat., n malignancies/N in group			
	I	II	III	IV
[5]	0/22	1/8	5/11	26/29
[15]	-	0/4	4/7	5/5
[16]	1/2	1/7	4/13	7/10
[17]	0/7	4/5	4/4	6/6
[18]	0/15*	-	29/49	18/18
[19]	-	3/28	8/29	-
[20]	-	-	28/179†	-
[21]	-	-	17/28	-
[23]	0/11	1/2	10/10	12/12
Total	1/57	10/54	109/330	74/80
% malignancy	1.7	18.5	33.0	92.5

TABLE 3

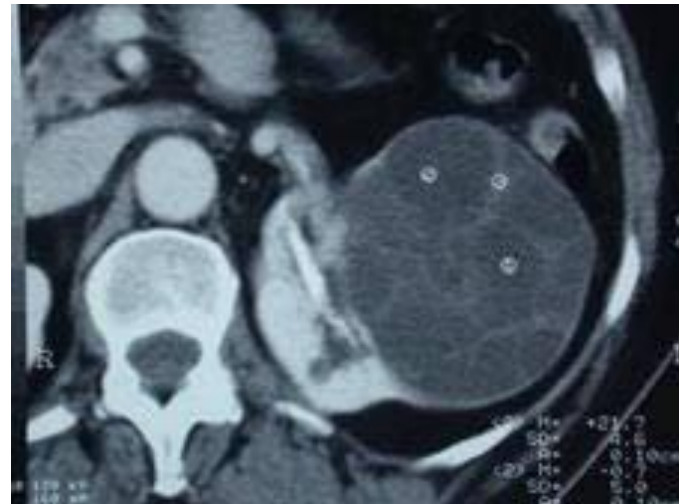
Summary of studies correlating pathology with Bosniak category

*category I and II combined;
†category II and IIF combined.



Renal cysts

BOSNIAK CLASSIFICATION



Renal cysts

BOSNIAK CLASSIFICATION



BOSNIAK I



BOSNIAK II



BOSNIAK III



BOSNIAK IV

Bosniak Renal Cyst Classification System

No further follow up



Follow Up imaging



Follow Up imaging



F-U vs. Surgery



Surgery



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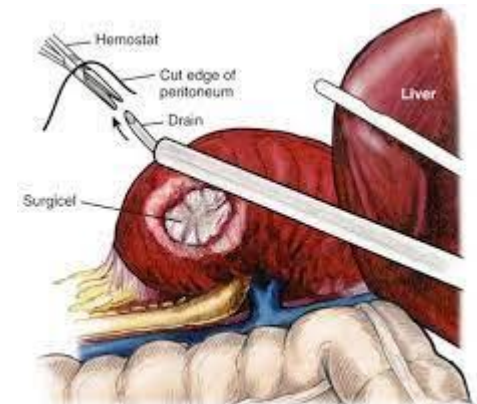
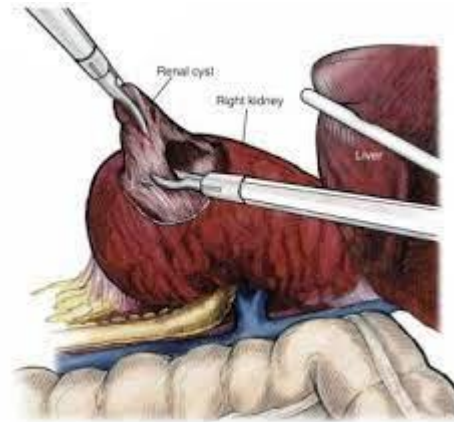
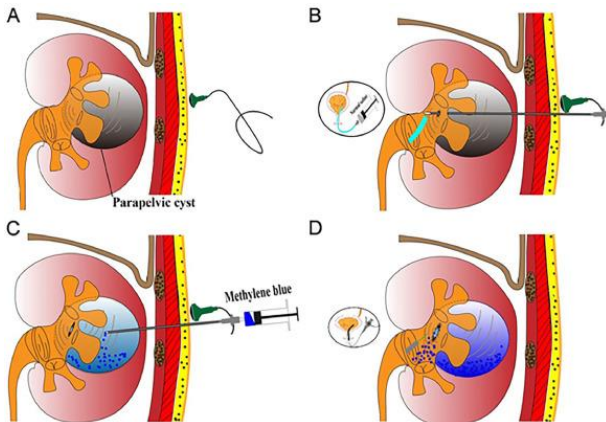
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Cystic mass with thickened irregular or smooth walls or septa in which measurable enhancement is present

- IV** - **Enhancing soft-tissue components**
Clearly malignant cystic masses that can have all of the criteria of category III but also contain distinct enhancing soft-tissue components independent of the wall or septa

Simple cysts Therapy

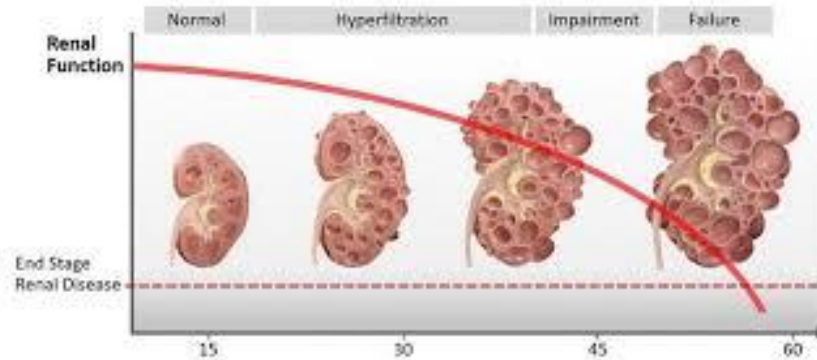
Only required if huge and/or symptomatic.

- ✓ Percutaneous alcohol ablation
- ✓ Laparoscopic marsupialization



Autosomal Dominant Polycystic Kidney Disease

Disease Progression in ADPKD



- ✓ The most prevalent inherited nephropathy.
- ✓ ADPKD accounts for 8% to 10% of patients receiving renal replacement transplant
- ✓ The disease is characterized by dysregulated growth of renal epithelial cells leading to **progressive, bilateral fluid-filled renal cysts**
- ✓ **End Stage Renal Disease** and dialysis in > 50% of cases

Benign renal tumors

Angiomyolipoma

- ✓ It is a benign renal neoplasm that is characterized by the presence of amounts of mature **fat tissue, smooth muscle and thick-walled blood vessels**;
- ✓ The most frequent benign neoplasm: incidence 0.5-2%;
- ✓ 20% diagnosed in patients with tuberous sclerosis (TS), 50% will develop an AML (penetrance is incomplete).
- ✓ The presence of dense adipose tissue is highly suggestive of AML; **a small proportion of adipose tissue virtually excludes the diagnosis of RCC**

Benign renal tumors

Angiomyolipoma

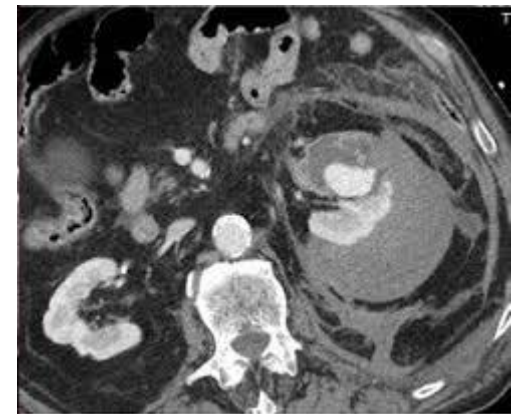
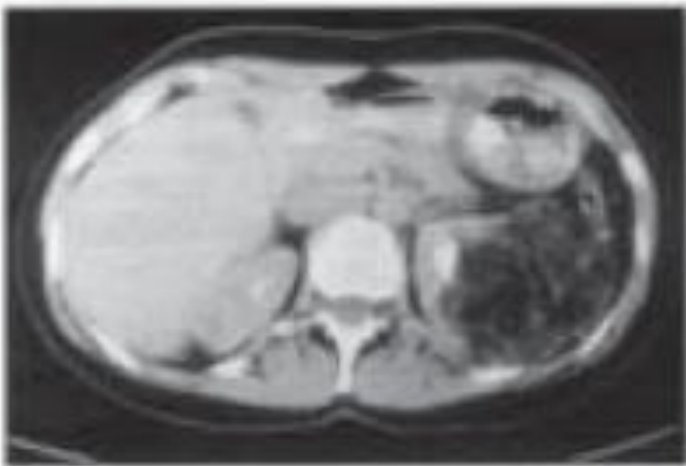


Hyperechoic ultrasonographic lesion

Angiomyolipoma

- Up to $\emptyset < 4$ cm, asymptomatic patients can be periodically checked.
- Symptomatic patients with voluminous lesions should be treated with embolization, tumorectomy or nephrectomy

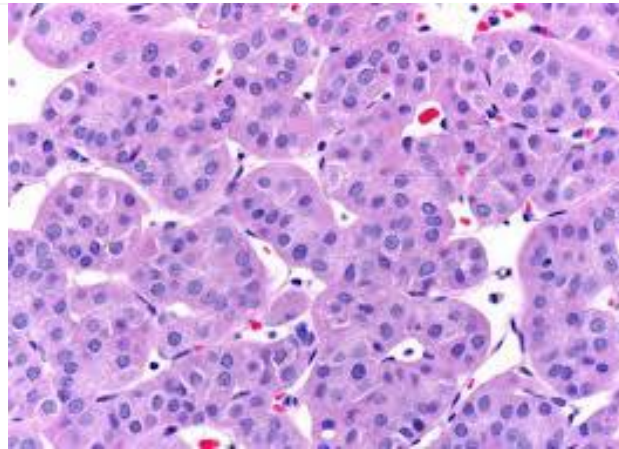
RISK OF SPONTANEOUS RUPTURE



Benign renal tumors

Oncocytoma

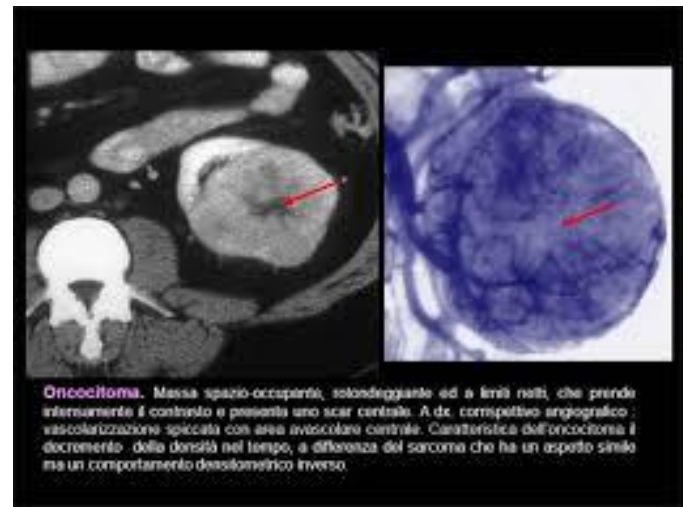
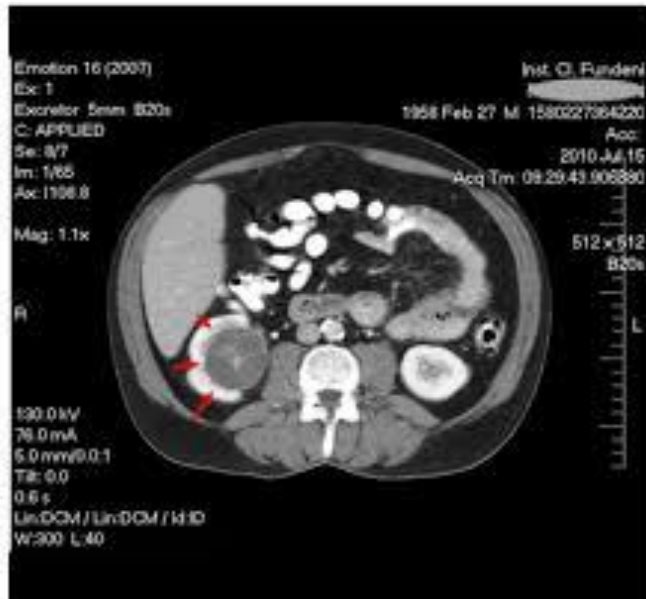
- ✓ Originates from the distal portion of the nephron (collector duct);
- ✓ 3-7% of all solid renal cancers.



Benign renal tumors

Oncocytoma

Lesion characterized by a **star-shaped central scar** (at CT) and by a **toothed wheel appearance** (at angiography)



Oncocytoma Therapy

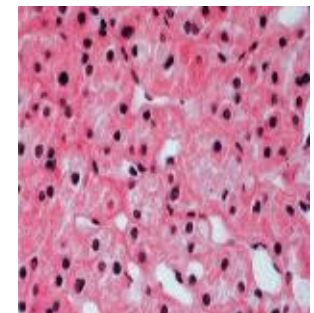
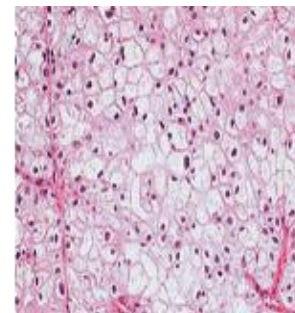
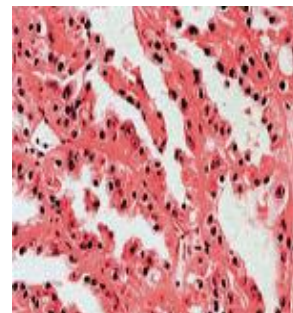
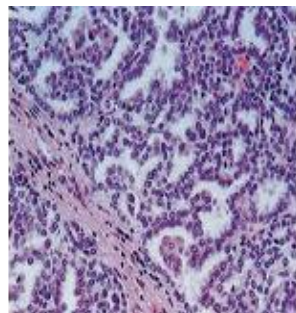
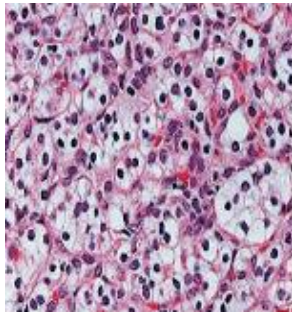
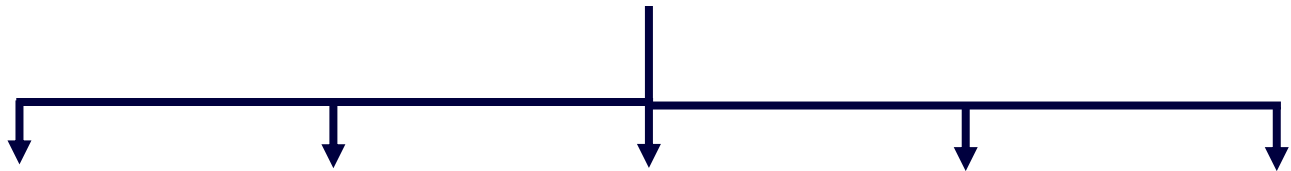
- ✓ Unfortunately, most renal **oncocytomas cannot be differentiated from RCC** based on clinical and radiological data only.
- ✓ Due to the un reliability of pre-operative diagnosis (included biopsy!), **a surgical approach is always recommended**

Histology: RCC is not one disease

*2016 WHO lists over 50 different types of kidney cancer

(Sarcomatoid variant can occur with any subtype)

Undifferentiated type and Collecting duct carcinoma constitute the other 2 types listed in AJCC classification



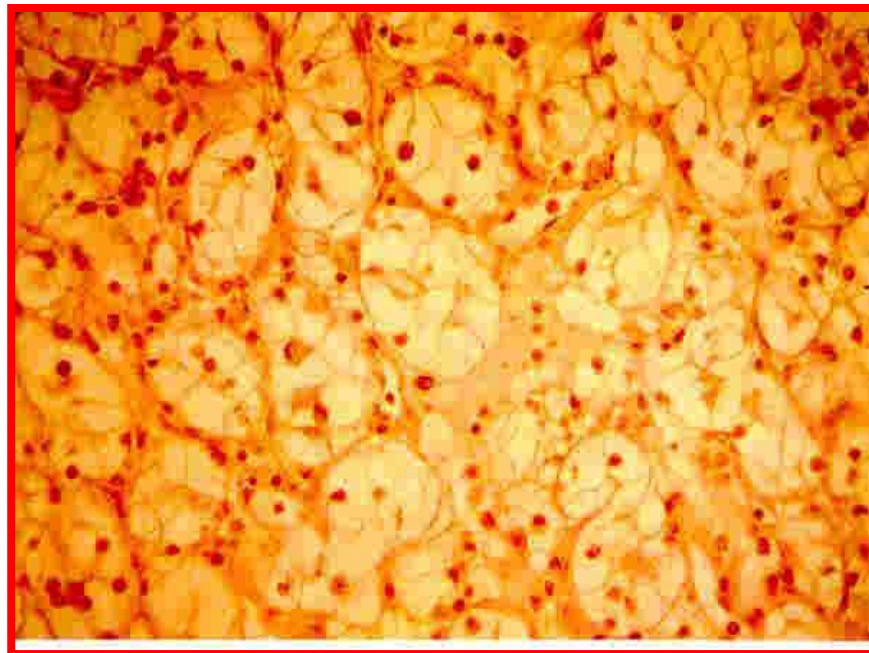
Type	Clear cell	Papillary type 1	Papillary type 2	Chromophobe	Oncocytoma
Incidence (%)	75%	5%	10%	5%	5%
Associated mutations	VHL	c-Met	FH	BHD	BHD

BHD=Birt-Hogg-Dubé; FH=fumarate hydratase; VHL= von Hippel-Lindau.

Modified from Linehan WM et al. *J Urol.* 2003;170:2163-2172.

RENAL CELL CARCINOMA HISTOLOGY

Clear cell renal cell carcinoma (ccRCC)



**Originates from the epithelium of the
distal tubules**

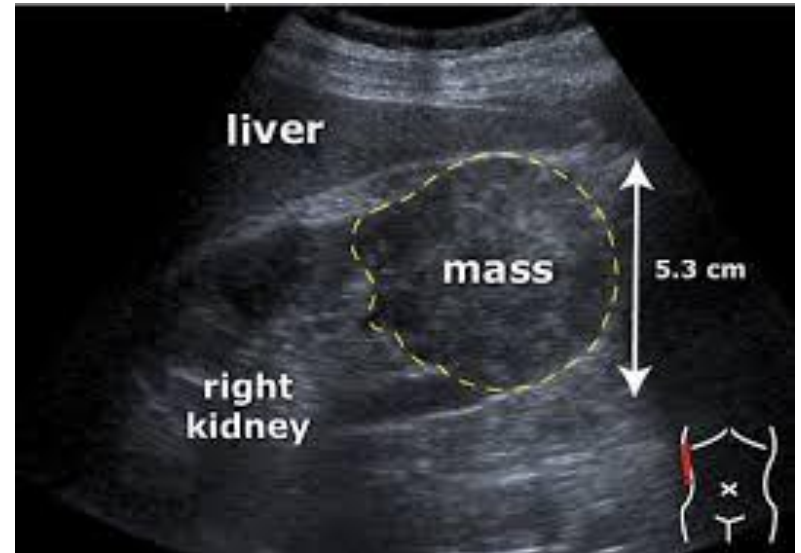
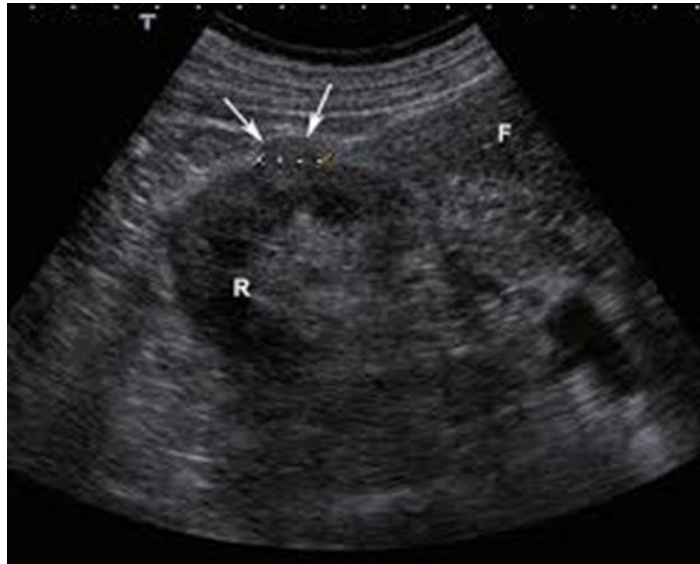
RENAL CELL CARCINOMA

- **DIAGNOSIS**
- STAGING
- GRADING
- TREATMENT
 - SMALL RENAL MASSES
 - LOCALLY ADVANCED DISEASE
 - METASTATIC

RENAL CELL CARCINOMA SYMPTOMS

Generally asymptomatic and incidentally diagnosed with **ultrasound**.

High **sensitivity** - High **specificity**.



When symptomatic....

	Occurrence among patients with symptomatic RCC	Proposed causes
Local symptoms		
1. FLANK PAIN, 2. HAEMATURIA, 3. PALPABLE ABDOMINAL MASS	Common	Urinary system obstruction or infiltration, invasion of adjacent organs, retroperitoneal space-occupying mass
	Less frequent	Urinary system infiltration
	Less frequent	Retroperitoneal space-occupying mass
	Rare	Increased venous pressure due to space-occupying mass or venous thrombus
Paraneoplastic disorders		
Hypertension	Common	Increased production of renin directly by tumour; compression or encasement of the renal artery or its branches causing renal artery stenosis; or arteriovenous fistula within the tumour, polycythaemia, hypercalcaemia, ureteral obstruction, and increased intracranial pressure associated with cerebral metastases
Anaemia	Common	Bleeding, abnormal production of prostaglandins, cytokines, and inflammatory mediators
Cachexia, weight loss	Common	Abnormal production of prostaglandins, cytokines, and inflammatory mediators
Pyrexia	Less frequent	Abnormal production of prostaglandins, cytokines, and inflammatory mediators
Raised hepatic enzyme concentrations in absence of liver metastases (Stauffer's syndrome)	Less frequent	Non-specific hepatitis associated with a prominent lymphocytic infiltrate, raised concentrations of interleukin-6 in serum
Hypercalcaemia	Less frequent	Osteolytic metastatic involvement of bone, production of parathyroid-hormone-like peptides, tumour-derived 1,25-dihydroxycholecalciferol, and prostaglandins
Polycythaemia	Rare	Increased production of erythropoietin directly by the tumour or by the adjacent parenchyma in response to hypoxia induced by tumour growth
Hypoglycaemia, neuromyopathy, amyloidosis, vascular thrombosis, Cushing's syndrome, protein enteropathy, galactorrhoea, gynaecomastia, decreased libido, hirsutism, amenorrhoea, chills, necrotising myopathy, immune thrombocytopenic purpura	Anecdotal	Abnormal production of 1,25-dihydroxycholecalciferol, renin, erythropoietin, prostaglandins, parathyroid-hormone-like peptides, lupus-type anticoagulant, human chorionic gonadotropin, insulin, various cytokines or inflammatory mediators
RCC=renal cell carcinoma.		
Table 1: Most frequent local symptoms and paraneoplastic disorders associated with RCC		

RENAL CELL CARCINOMA SYMPTOMS

The Classic Triad

- ✓ **FLANK PAIN** and
- ✓ **MACROSCOPICA HAEMATURIA** and
- ✓ **PALPABLE ABDOMINAL MASS**

... is today a rare presentation (6-10%) and correlates with aggressive histology and advanced disease

When symptomatic....

	Occurrence among patients with symptomatic RCC	Proposed causes
Local symptoms		
Acute or chronic flank pain	Common	Urinary system obstruction or infiltration, invasion of adjacent organs, retroperitoneal space-occupying mass
Gross haematuria	Less frequent	Urinary system infiltration
Palpable abdominal mass	Less frequent	Retroperitoneal space-occupying mass
Varicocele	Rare	Increased venous pressure due to space-occupying mass or venous thrombus
Paraneoplastic disorders		
Blood hypertension	Common	Increased production of renin directly by tumour; compression or encasement of the renal artery or its branches causing renal artery stenosis; or arteriovenous fistula within the tumour, polycythaemia, hypercalcaemia, ureteral obstruction, and increased intracranial pressure associated with cerebral metastases
	Common	
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RENAL CELL CARCINOMA PARANEOPLASTIC SYMPTOMS

HYPERCALCEMIA (10%)

Peptide similar to parathormonal agent

HYPERTENSION

Overproduction of renin

POLYCYTHEMIA

Overproduction of erythropoietin

RENAL CELL CARCINOMA PARANEOPLASTIC SYMPTOMS

Stauffer syndrome

- ✓ Liver functional tests alteration
 - ✓ Leucopenia
 - ✓ Fever

Aetiology

?

RENAL CELL CARCINOMA

SYMPTOMS related to METASTASES

More rarely clinical manifestation with signs due to metastatic localizations

- ✓ **Bone pain**
- ✓ **Neurological syndrome**

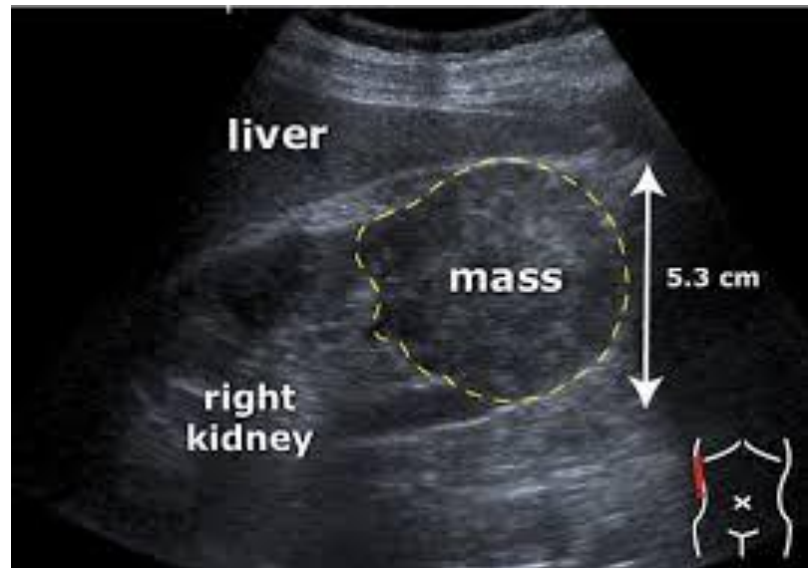


FIGURE 3. CT showing lytic lesion of the right ischium.

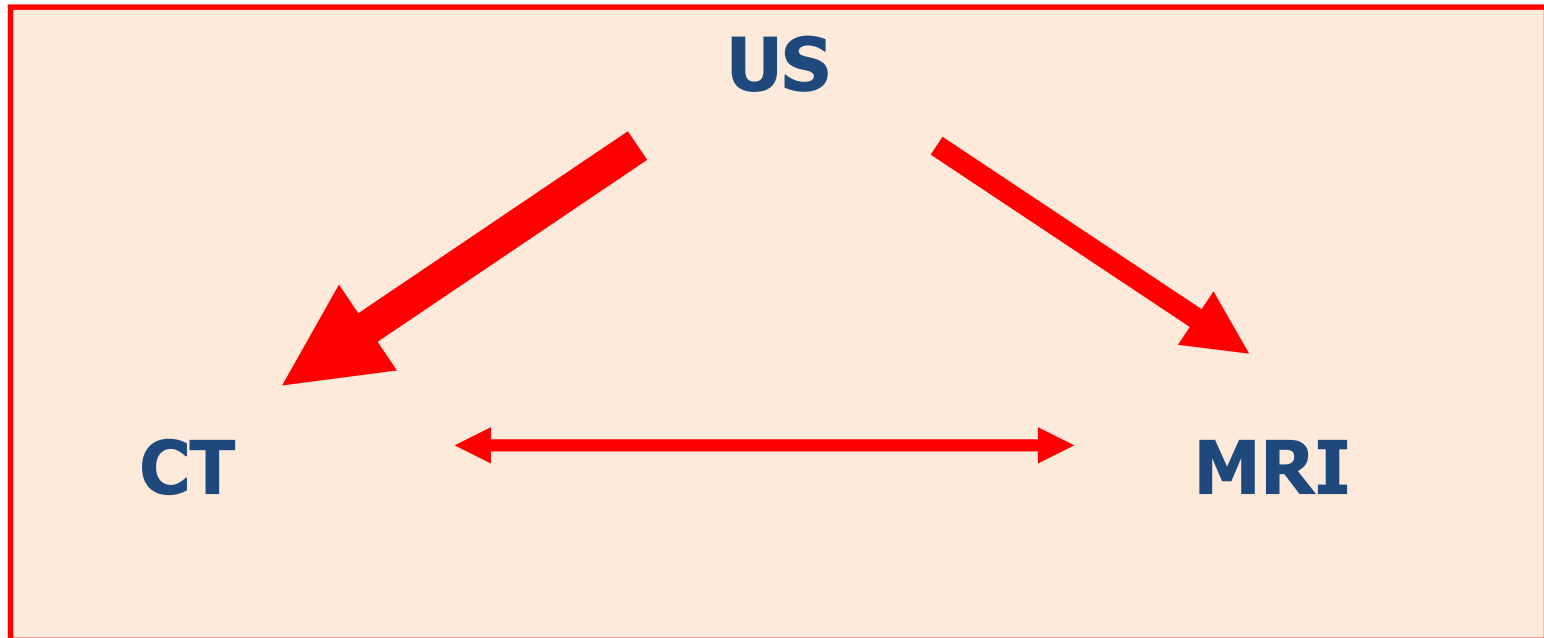


RENAL CELL CARCINOMA DIAGNOSIS

More than 50% of RCCs are detected **incidentally** by non-invasive imaging (**ULTRASONOGRAPHY**) investigating various non-specific symptoms and other abdominal diseases

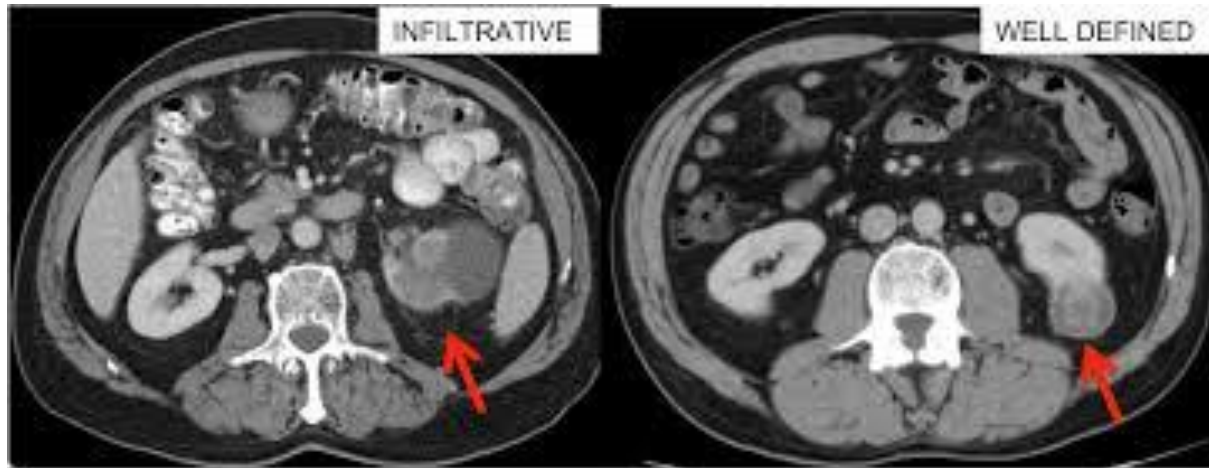


RENAL CELL CARCINOMA DIAGNOSIS

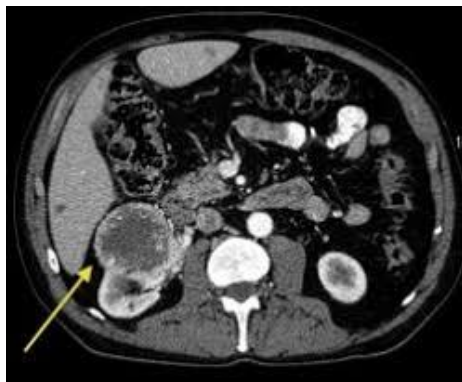


RENAL CELL CARCINOMA

CT DIAGNOSIS

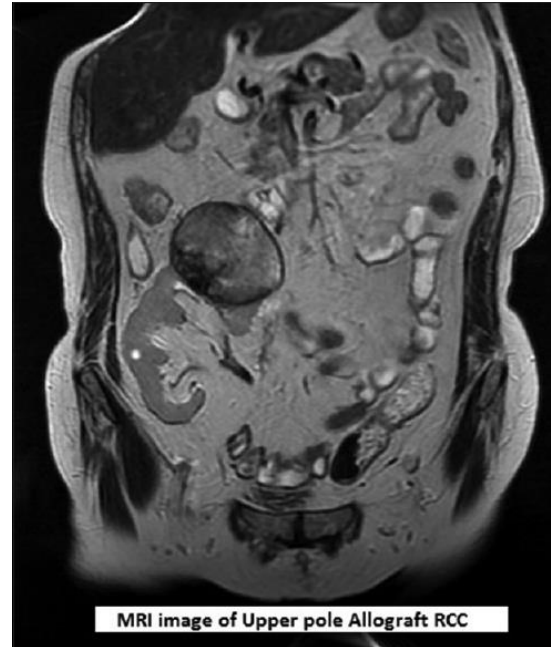
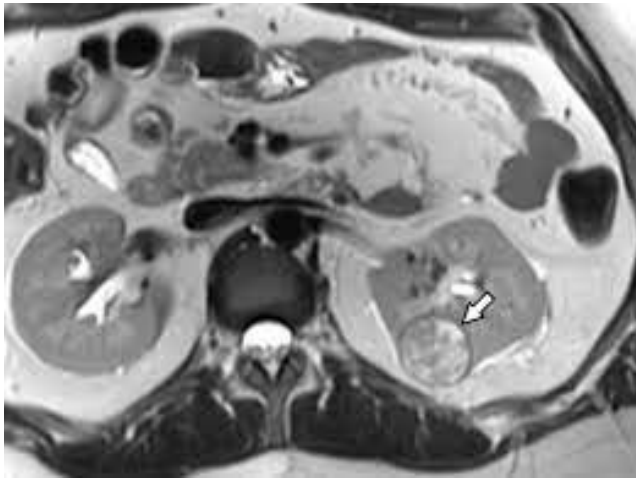


Staging rather than diagnosis
High sensitivity and specificity



RENAL CELL CARCINOMA

MRI DIAGNOSIS



Only if:

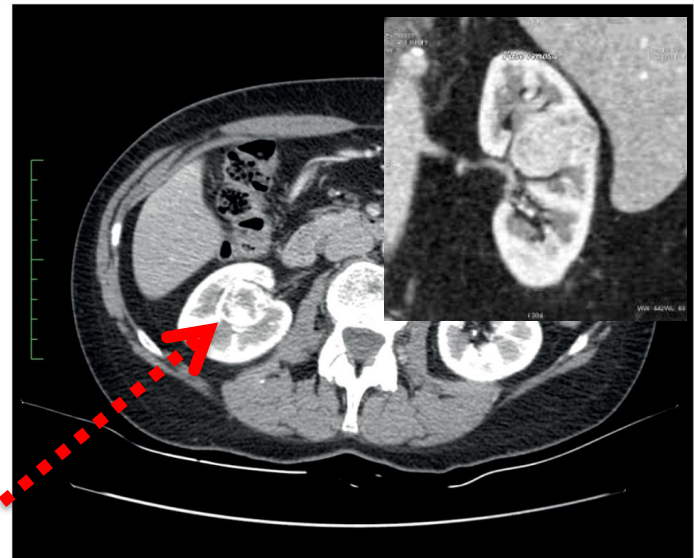
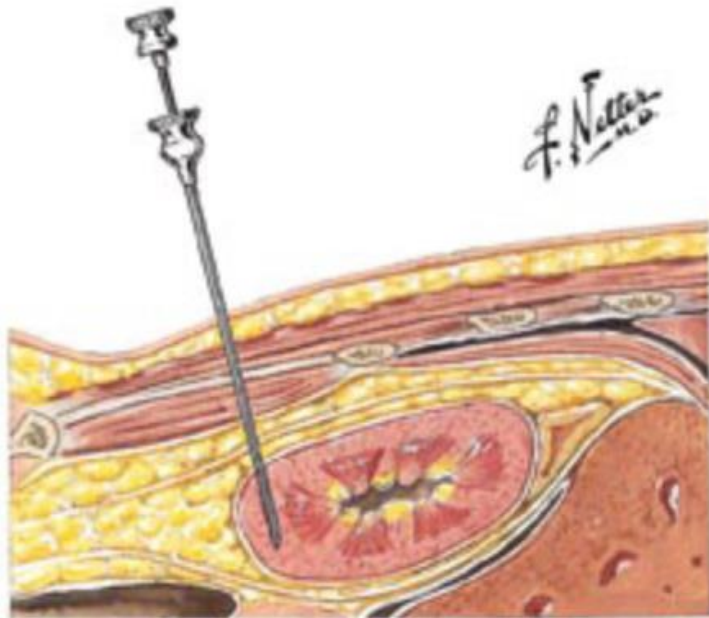
- ✓ Impaired renal function
- ✓ Contrast allergy

Do we need a biopsy to confirm the diagnosis?

NO!

Ecoguided percutaneous biopsy only in special cases

- ✓ Active surveillance
- ✓ Small masses which do not allow conservative surgery.



CT scan showing a small (intrarenal) mass of the right kidney. Percutaneous biopsy revealed the presence of renal oncocytoma

RENAL CELL CARCINOMA

- DIAGNOSIS
- **STAGING**
- GRADING
- TREATMENT
 - SMALL RENAL MASSES
 - LOCALLY ADVANCED DISEASE
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RCC – TNM (Tumour Nodes Metastases)

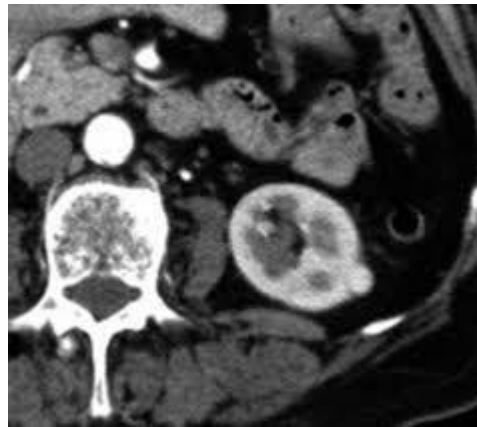
T - Primary Tumour

- TX Primary tumour cannot be assessed
- T0 No evidence of primary tumour
- T1 Tumour \leq 7 cm or less in greatest dimension, limited to the kidney
 - T1a Tumour \leq 4 cm or less
 - T1b Tumour $>$ 4 cm but \leq 7 cm
- T2 Tumour $>$ 7 cm in greatest dimension, limited to the kidney
 - T2a Tumour $>$ 7 cm but \leq 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)

RENAL CELL CARCINOMA TUMOR STAGING

Stage T1 a-b

Limited to the Kidney - diameter < 7 cm



T1a < 4 cm



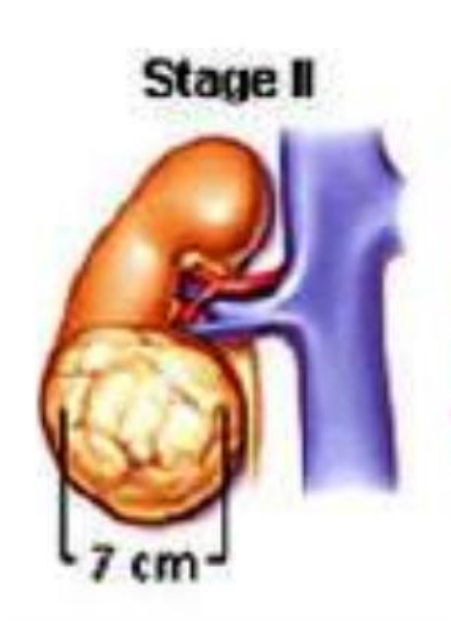
T1b > 4 cm

RENAL CELL CARCINOMA TUMOR STAGING

Stage T2

Limited to the Kidney - diameter > 7 cm

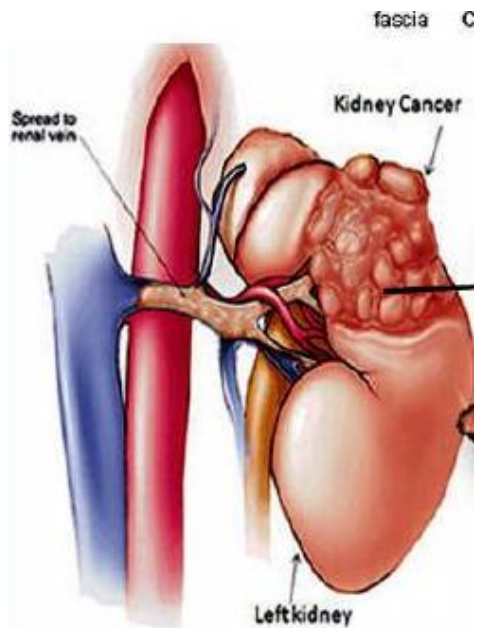
T2a > 7 cm – **T2b** > 10 cm



RENAL CELL CARCINOMA TUMOR STAGING

Stage T3a

- ✓ Renal vein invasion
- ✓ Perinephric tissues invasion



RENAL CELL CARCINOMA TUMOR STAGING

Stage T3b

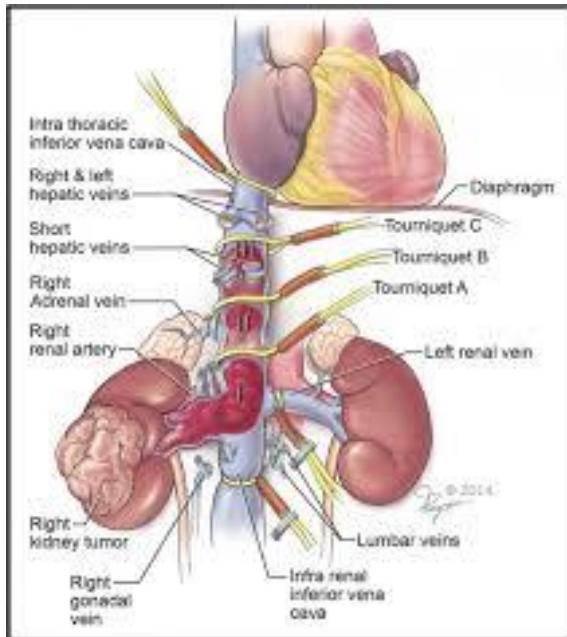
- ✓ **Vena cava invasion** below the diaphragm



RENAL CELL CARCINOMA TUMOR STAGING

Stage T3c

✓ **Vena cava invasion** above the diaphragm



RENAL CELL CARCINOMA

TUMOR STAGING

Stage T4

- ✓ Tumour invades beyond the Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)



RENAL CELL CARCINOMA

Nodes and Metastases STAGING

N - Regional Lymph Nodes

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Metastasis in regional lymph node(s)

Less frequent

M - Distant Metastasis

- M0 No distant metastasis
- M1 Distant metastasis

More frequent

RENAL CELL CARCINOMA

Lymph nodes invasion

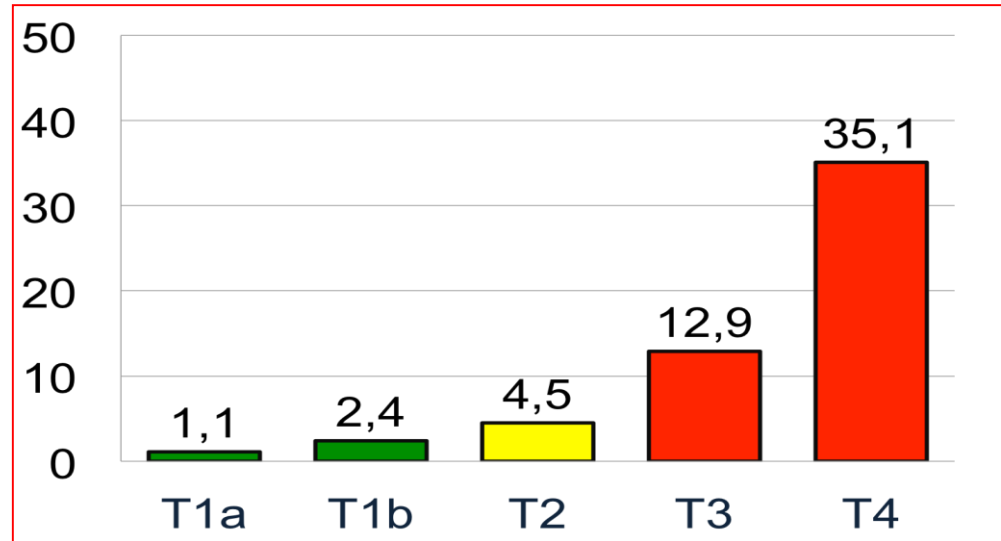


Table 2 – Pathologic N1 prevalence within clinical, surgical, and pathologic features proposed as predictors of regional lymph node involvement at nephrectomy*

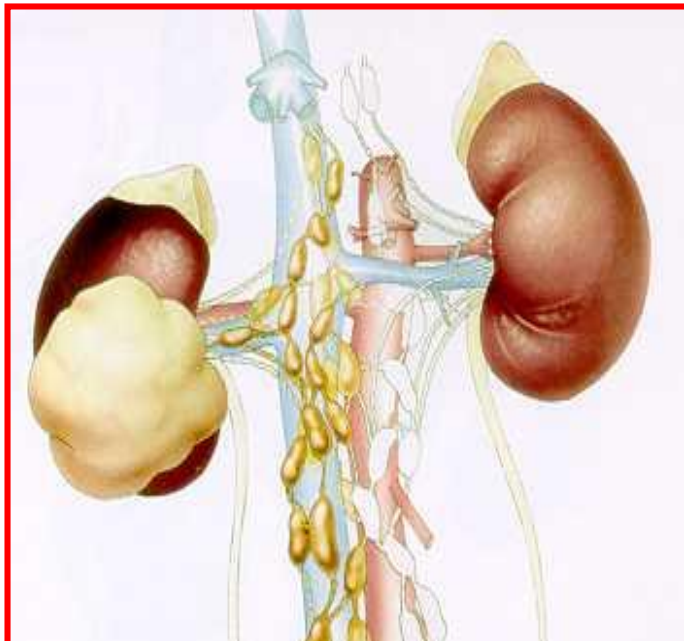
Variable	Blute et al. [31]	Capitanio et al. [28]	Pantuck et al. [6]	Whitson et al. [44]
pT				
1	2.3	1.1	2.4	5.1
2	3.6	4.5	11.4	11.1
3–4	37.1	12.3	30.6	31.0
Fuhrman grade				
I–II	0.6	NA	6.3	7.2
III–IV	8.8	NA	26.0	30.8
Symptomatic at presentation	5.2	NA	NA	NA
Tumor thrombus	8.8	NA	NA	NA
Coagulative tumor necrosis	11.1	NA	NA	NA
Sarcomatoid component	27.5	NA	32.3	NA

NA = not applicable.

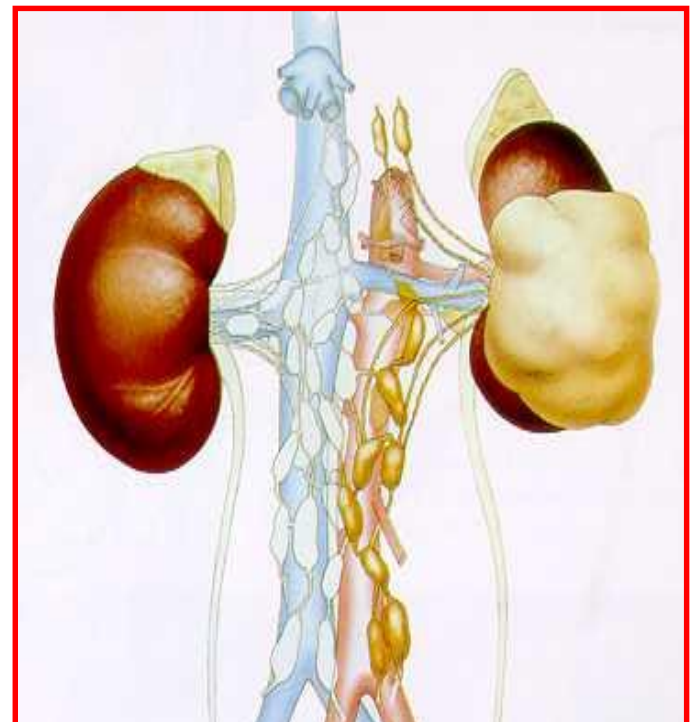
* Only series published in the last decade were considered.

RENAL CELL CARCINOMA

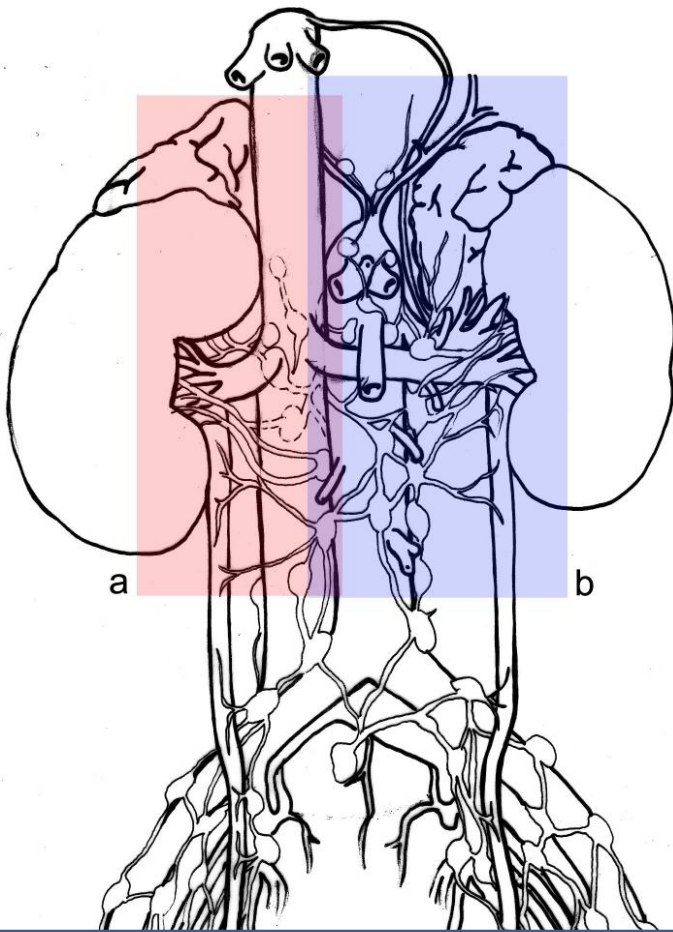
Nodes STAGING



precaval
inter-aorto-caval



pre and para-aortic



Predilection of RCC for early haematogenic dissemination
 ≈57% TanyN0M1

Directly to the thoracic duct
 ≈30%

many possible different lymphatic routes
 in normal retroperitoneal anatomy

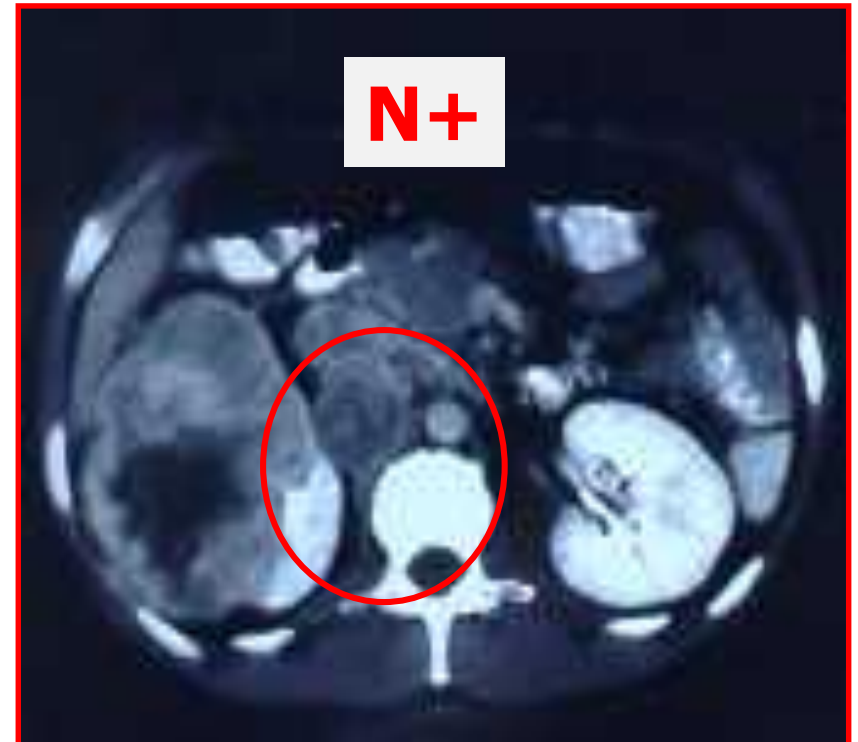
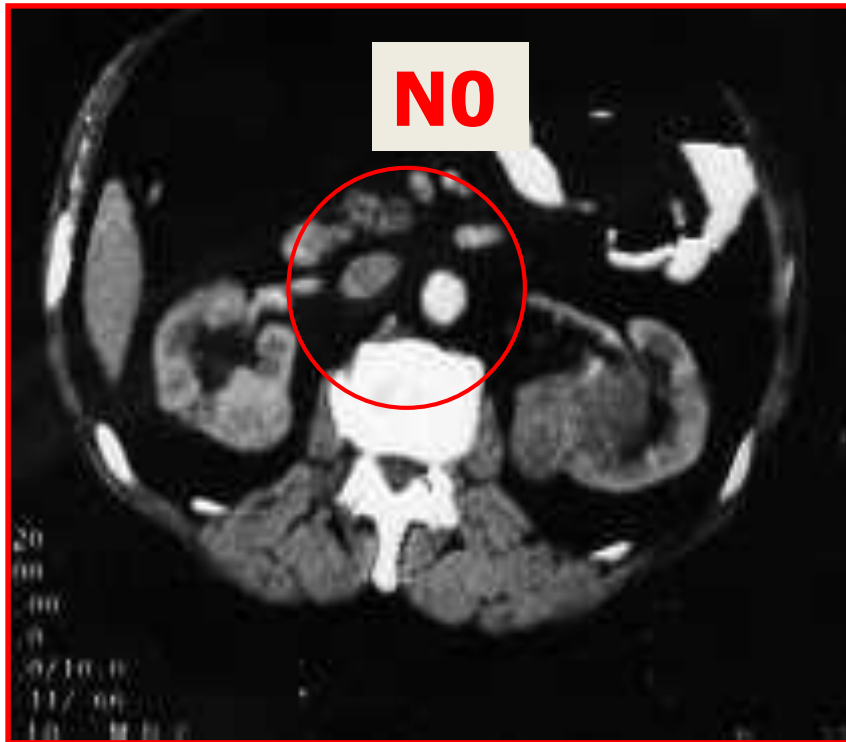
collateral lymphatic drainage and
 invasion of tissue with different
 lymphatic drainage (e.g. perinephric fat).

Isolated metastases in the
 ipsilateral iliac and
 supraclavicular nodes
 ≈10%

N - Regional LNs	
NX	Regional LNs cannot be assessed
N0	No regional LN metastasis
N1	Regional LN metastasis

RENAL CELL CARCINOMA

CT Nodal Staging STAGING

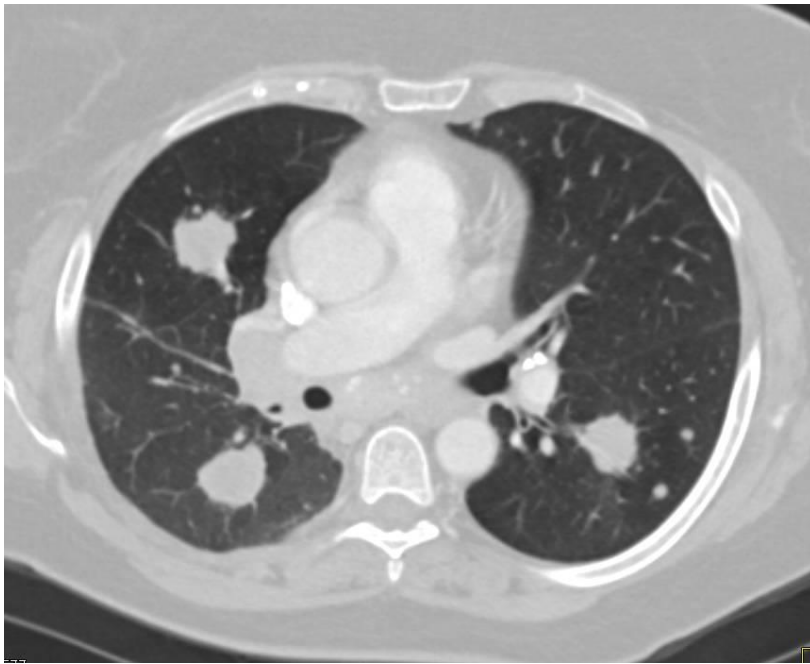


Low sensitivity

High specificity

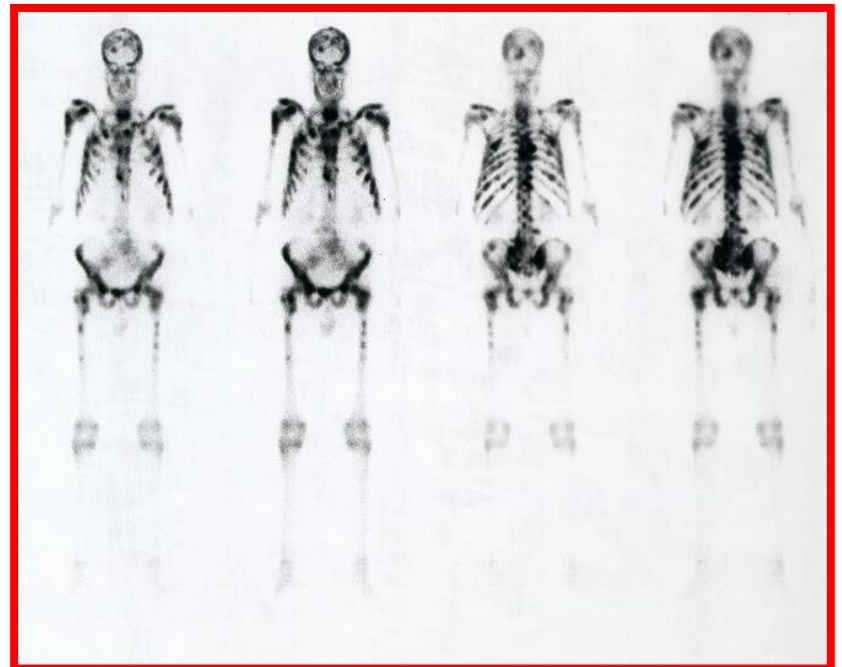
RENAL CELL CARCINOMA

Metastases Staging



Lungs

CT high sensibility and specificity



Bones

Bone scan

RENAL CELL CARCINOMA

Metastases Staging

Brain

Contralateral adrenal gland

Liver

Skin

Pancreas

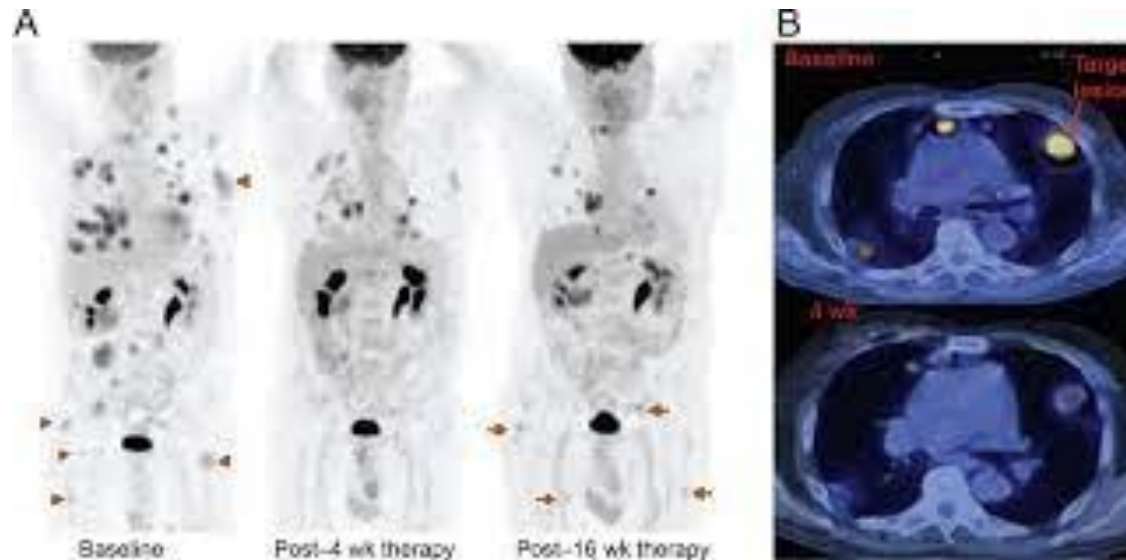
Ureter

Testis



RENAL CELL CARCINOMA

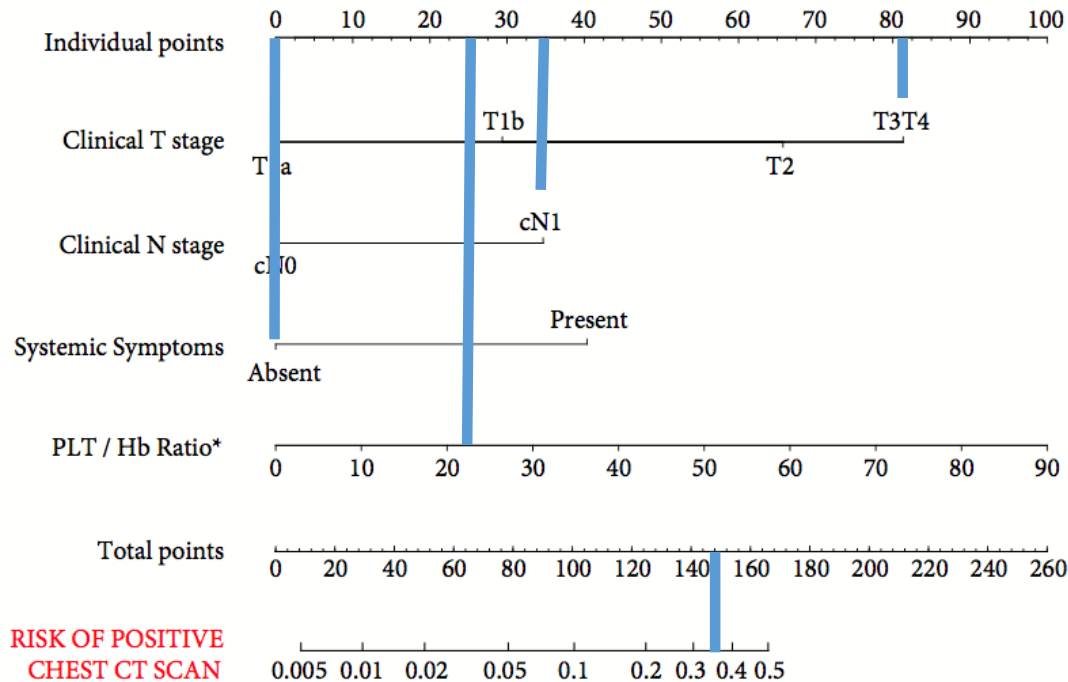
Metastases Staging



The application of **FDG PET/CT** is **limited for RCC**, mainly due to physiological excretion of FDG from the kidneys, which decreases contrast between renal lesions and normal tissue, and may obscure or mask the lesions of the kidneys.

When to perform preoperative chest computed tomography for renal cancer staging

Alessandro Larcher^{*†}, Paolo Dell'Oglio^{*†}, Nicola Fossati^{*†}, Alessandro Nini^{*†}, Fabio Muffin^{*†}, Nazareno Suardi^{*†}, Francesco De Cobelli[‡], Andrea Salonia^{*†}, Alberto Briganti^{*†}, Xu Zhang[§], Francesco Montorsi^{*†}, Roberto Bertini^{*†} and Umberto Capitanio^{*†}

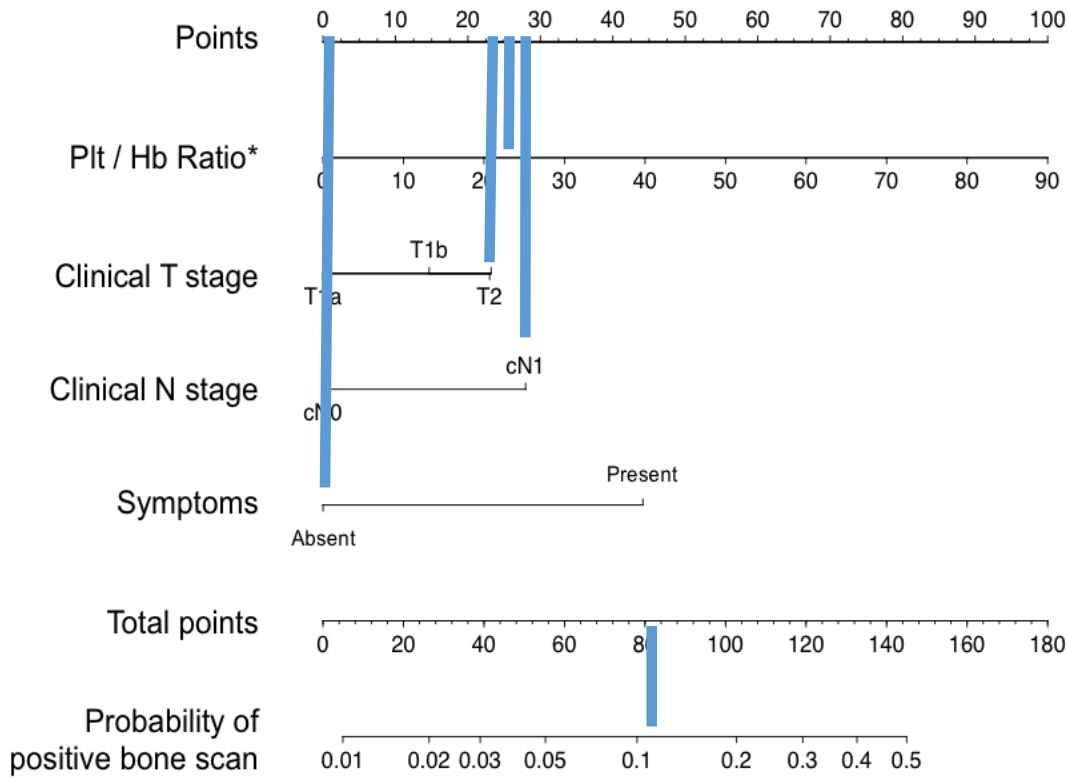


RISK of positive Chest CT scan= 38%



*Defined as the ratio between platelets count ($10^9/L$) and serum haemoglobin (g/dL).

When to Perform Preoperative Bone Scintigraphy for Kidney Cancer Staging



RISK of positive Bone scan= 12%

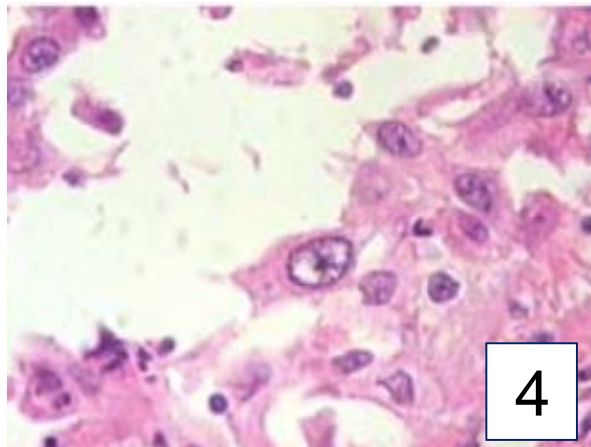
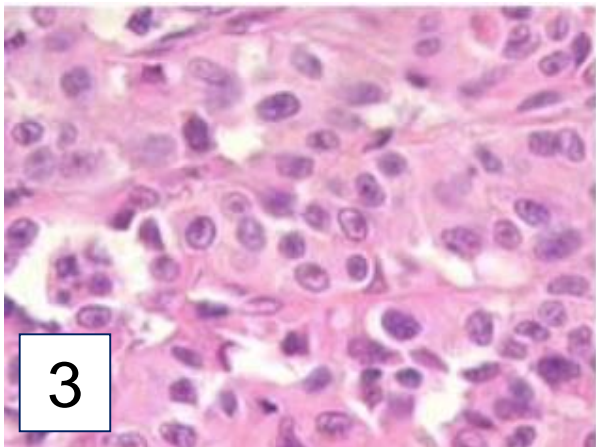
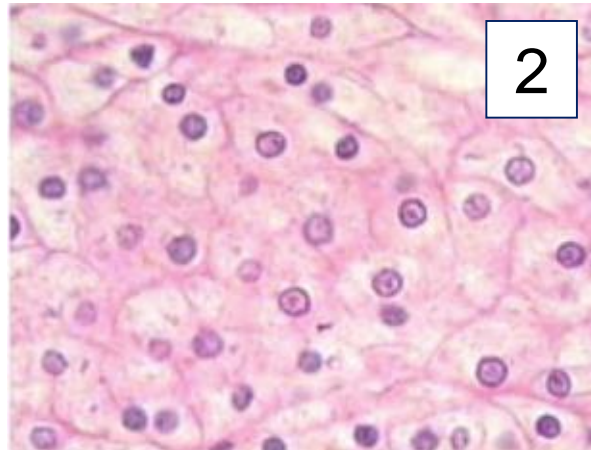
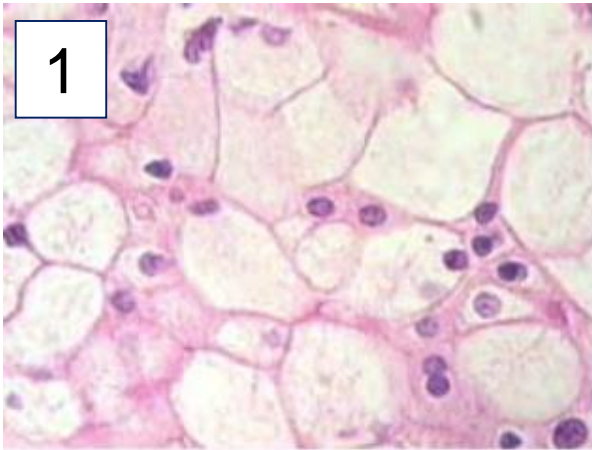


RENAL CELL CARCINOMA

- DIAGNOSIS
- STAGING
- **GRADING**
- TREATMENT
 - SMALL RENAL MASSES
 - LOCALLY ADVANCED DISEASE
 - METASTATIC

The **Fuhrman classification system** for nuclear grade (grade 1, 2, 3 and 4) has been the most generally accepted classification and independent predictor of survival in RCC setting

LOW INTER-OBSERVER REPRODUCIBILITY

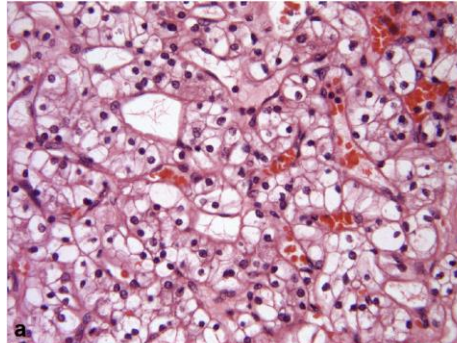


- Nuclei
- Nucleoli
- Sarcomatoid features

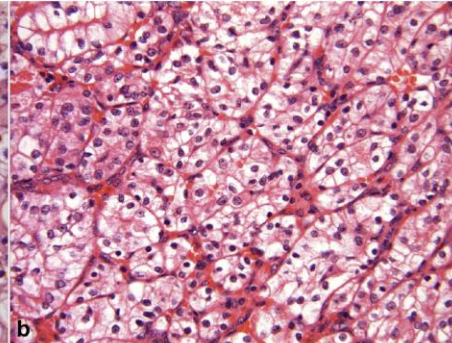
Table 1 – The International Society of Urological Pathology grading classification for renal cell carcinoma

Grade	Definition
1	Tumour cell nucleoli invisible or small and basophilic at $\times 400$ magnification
2	Tumour cell nucleoli conspicuous at $\times 400$ magnification but inconspicuous at $\times 100$ magnification
3	Tumour cell nucleoli eosinophilic and clearly visible at $\times 100$ magnification
4	Tumours showing extreme nuclear pleomorphism and/or containing tumour giant cells and/or the presence of any proportion of tumour showing sarcomatoid and/or rhabdoid dedifferentiation

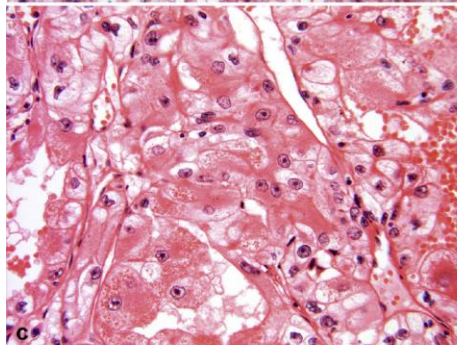
Grade 1



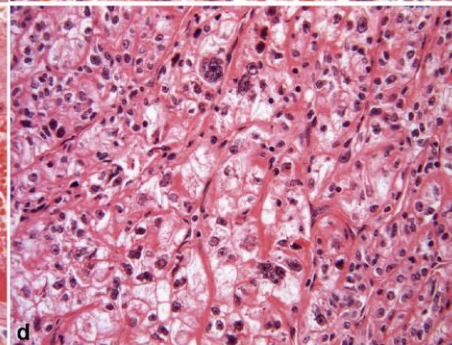
Grade 2



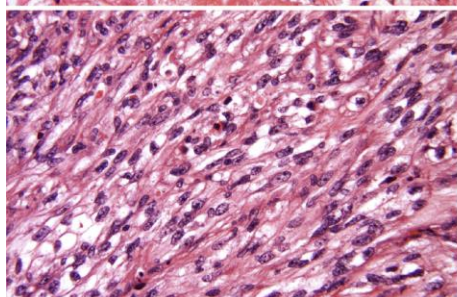
Grade 3



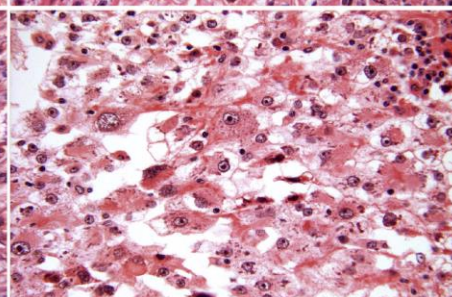
Grade 4



Grade 4



Grade 4



RENAL CELL CARCINOMA

- DIAGNOSIS
- STAGING
- GRADING
- **TREATMENT**
 - SMALL RENAL LOCALISED MASSES (T1-T2)
 - LOCALLY ADVANCED DISEASE (T3-T4)
 - METASTATIC (M+)

RENAL CELL CARCINOMA TREATMENT

- LOCALISED DISEASE (T1-T2)
- LOCALLY ADVANCED DISEASE (T3-T4)
- METASTATIC (M+)

RENAL CELL CARCINOMA LOCALISED DISEASE TREATMENT

1. Active Surveillance

2. Focal Therapy (radiofrequency ablation, cryoablation,
microwave ablation, stereotatic body radiotherapy)

3. Surgery (Radical Nephrectomy, Nephron sparing surgery) OPEN,
LAPAROSCOPIC, ROBOTIC

RENAL CELL CARCINOMA

Surgical Treatment T1-T2

THE RESULTS OF RADICAL NEPHRECTOMY FOR RENAL CELL CARCINOMA

CHARLES J. ROBSON, BERNARD M. CHURCHILL AND WILLIAM ANDERSON

*From the Division of Urology, Departments of Surgery and Pathology,
University of Toronto, Ontario, Canada*

(Reprinted from J. Urol, 101: 297-301, 1969)

Radical nephrectomy (according to Robson C et al, 1969):

- Kidney
- Perinephric fat and Gerota
- Ipsilateral adrenal gland
- Retroperitoneal lymph nodes



Charles J. Robson

Radical Nephrectomy

Vari tipi di incisioni per eseguire una nefrectomia radicale



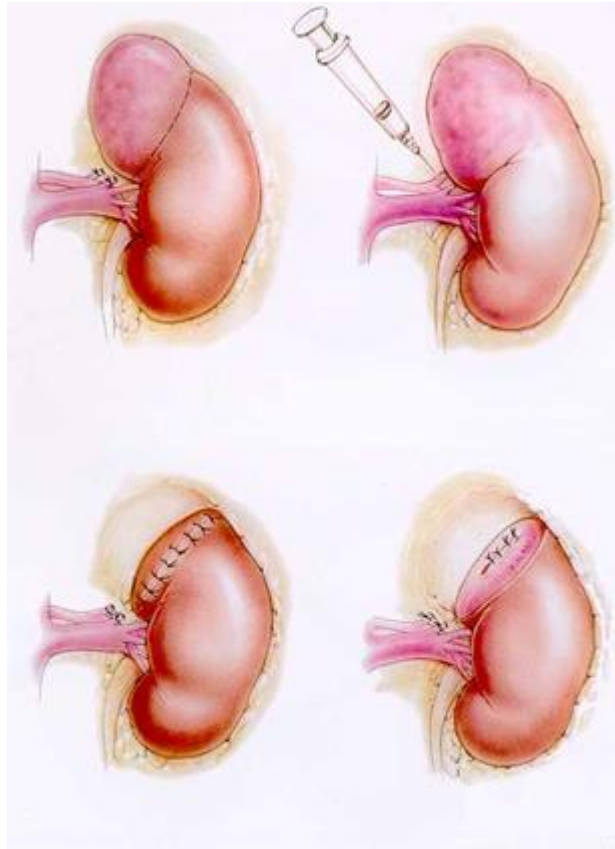
Gold standard:
laparoscopic when feasible



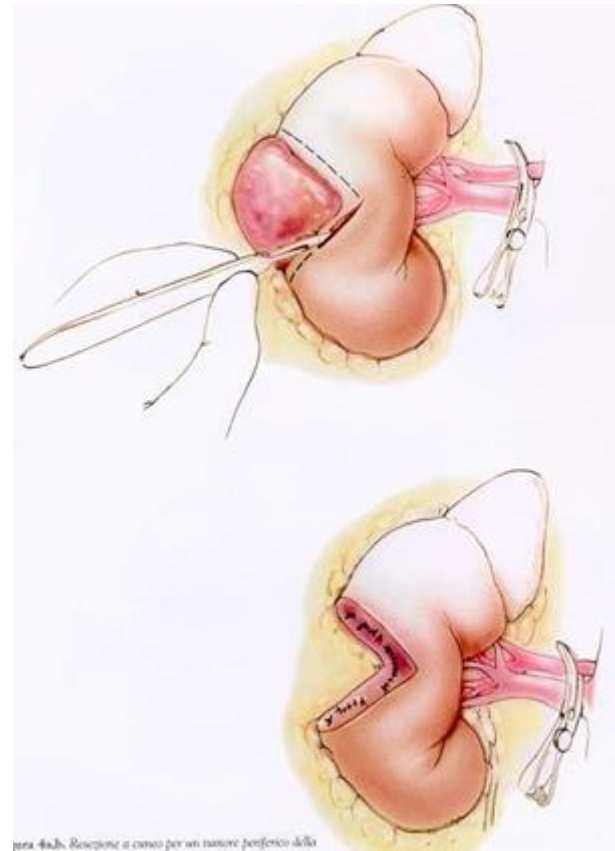
**IN RENAL CANCER,
SHOULD WE REMOVE THE
ENTIRE ORGAN?**



Nephron Sparing Surgery

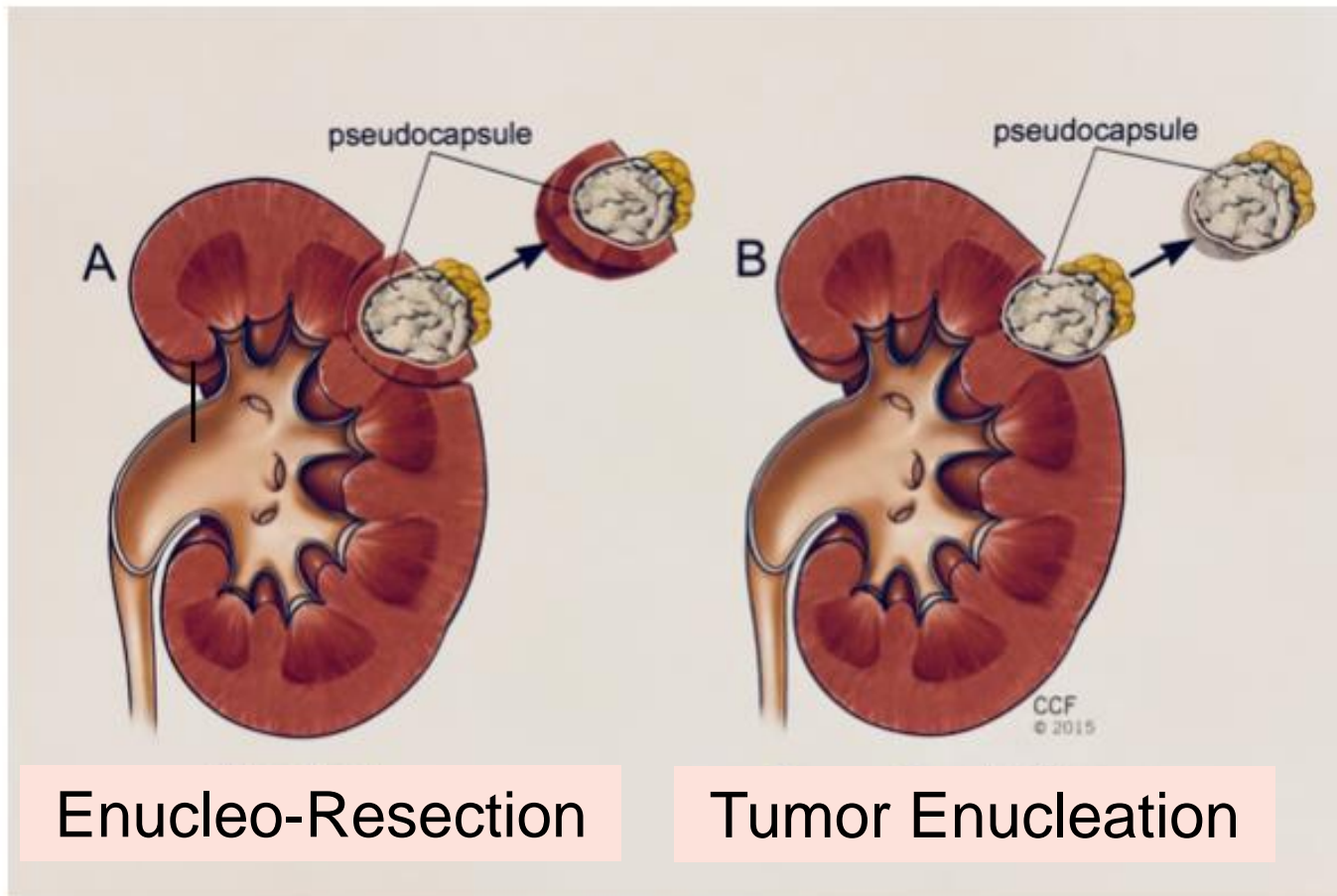


Partial Nephrectomy



Wedge Resection

Nephron Sparing Surgery



NSS VS. RN – CANCER SPECIFIC SURVIVAL

Prospective randomized EORTC Phase III 30904 trial showed

NO DIFFERENCE between NSS vs. RN

in patients with solitary T1-2 N0 M0 RCC <5 cm, normal contralateral kidney function and PS 0-2

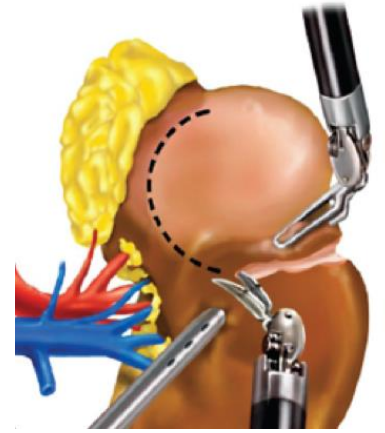
OUTCOME	PN	RN	HR (95% C.I.)
10-YEARS OVERALL SURVIVAL	75.7%	81.1%	1.5 (1.03 - 2.16)
CANCER SPECIFIC SURVIVAL	98.5%	97%	2.06 (0.62 - 6.81)
10-YEARS DISEASE FREE SURVIVAL	96.7%	95.5%	1.37 (0.58 - 3.24)

DEATHS DUE TO RCC



2.2% (n=12)

Nephron Sparing Surgery



When

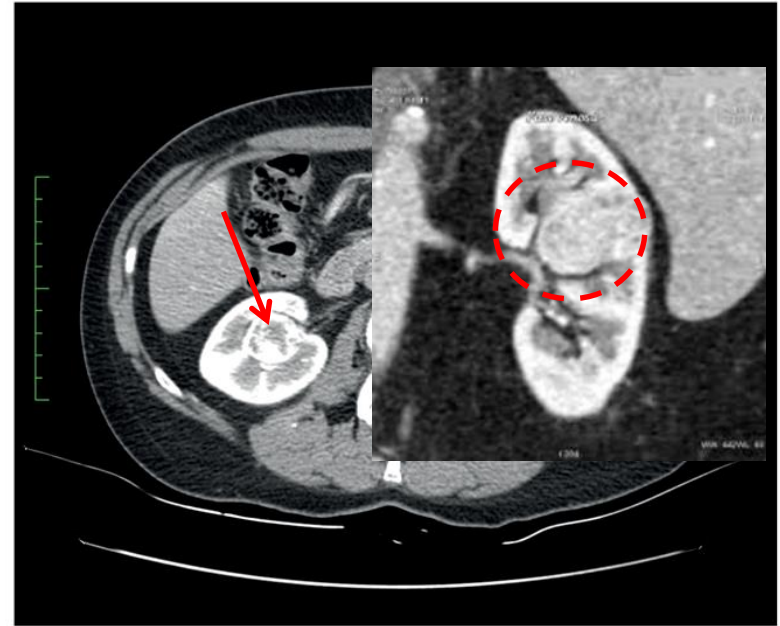
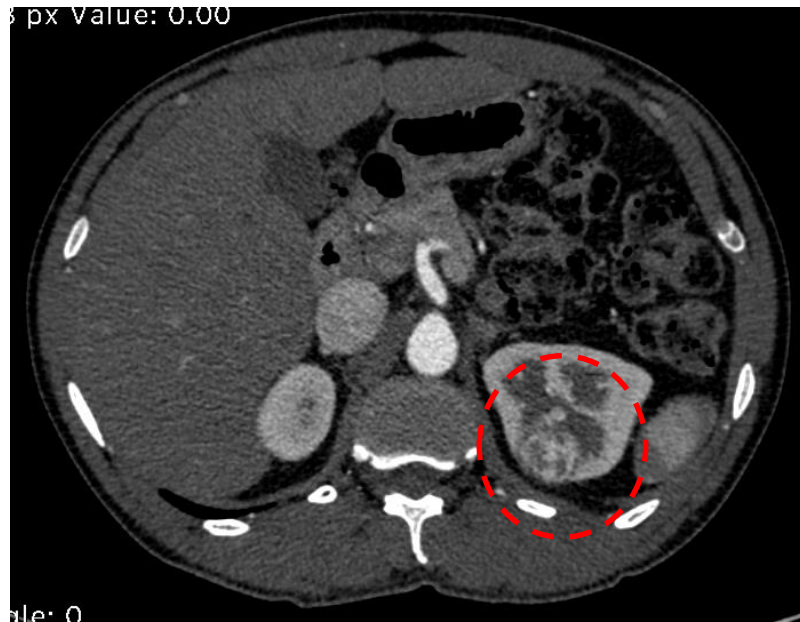
How

Why

Nephron Sparing Surgery: when?

- ✓ A *nephron-sparing* surgery is recommended in all renal masses with diameter < 5 cm (T1a)
- ✓ It can be considered, if technically feasible, in all neoplasms in the clinical stage T1b (up to 7 cm)

Nephron Sparing Surgery? cT1a



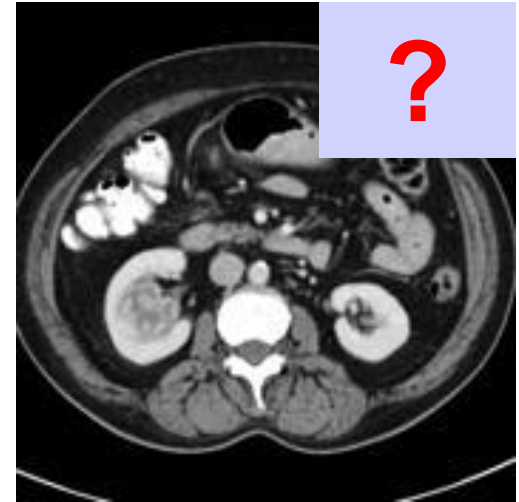
*CT scan showing a small (intrarenal) mass of the right kidney.
Percutaneous biopsy revealed the presence of renal oncocytoma*

- **Stage-migration** over the years
- Usually asymptomatic, **incidentally detected**
- Roughly **80%** of new RCC diagnosis are cT1-2 N0 M0

Surgical treatment T1-T2 renal cancer

Diameter < 5 cm

Nephron sparing surgery



Diameter > 7 cm

Radical nephrectomy



Nephron Sparing Surgery: when?

Stage T2

diameter > 7 cm T2a > 7 cm – T2b > 10 cm



Technically feasible and mandatory in particular cases (e.g. single kidney neoplasm)

Nephron Sparing Surgery

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

The real life: 'Overuse' of radical nephrectomy!

**Community
hospitals**

65000 RCC cases diagnosed in 2012

60% of those were small renal masses

39000 PN candidates

49% treated with PN

**Tertiary care
center**

90% treated with PN
(MSKCC, 2007)

Nephron Sparing Surgery

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

Always surgery?

TREATMENT

1- **Active Surveillance**

2- **Focal Therapy** (radiofrequency ablation,

cryoablation, microwave ablation, stereotatic body radiotherapy)

3- **Surgery** (Radical Nephrectomy, Nephron sparing surgery)

OPEN, LAPAROSCOPIC, ROBOTIC

SURVEILLANCE

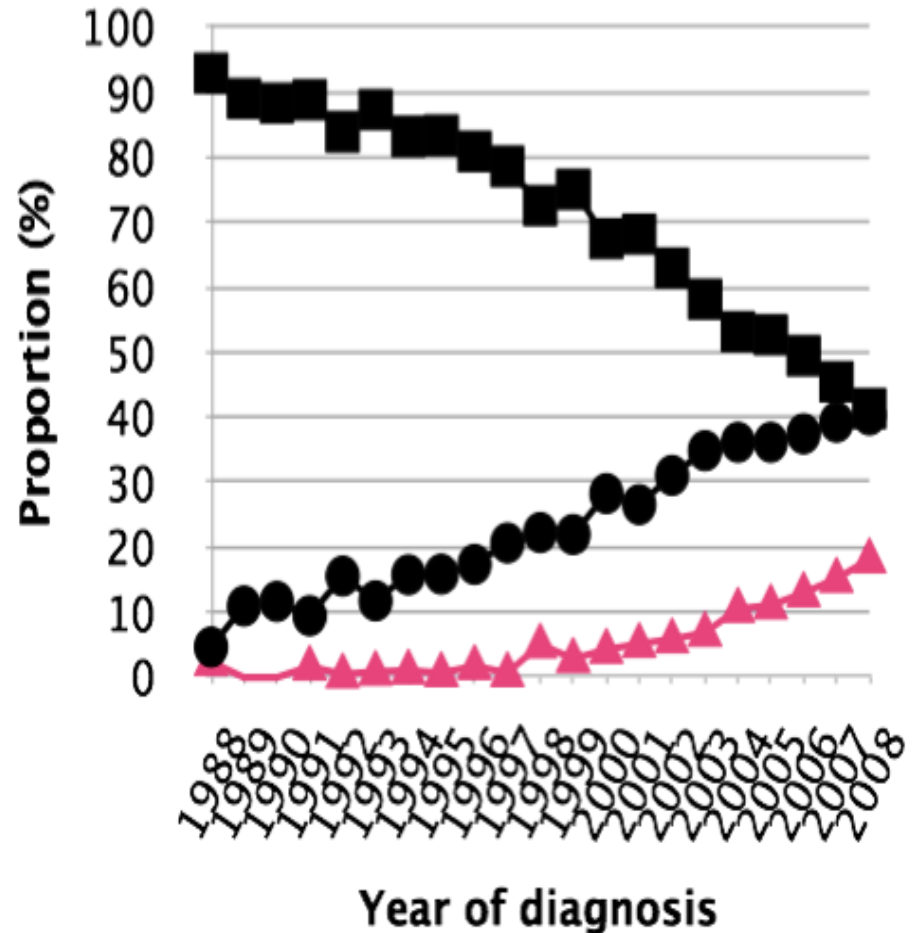
- 20–30% have benign pathology
- Slow growth (2–3 mm/yr)
- Low risk of metastatic progression (<1%)
- Delayed surgery does not increase oncological risk
- Lack of pathological confirmation
- Existing AS series: small sample size and short follow-up
- Lack of consensus on imaging technique and most optimal follow-up
- Cumulative radiation risk and increased costs

CONTEMPORARY MANAGEMENT OF KIDNEY CANCER

ACTIVE SURVEILLANCE

2–18%

Use of active surveillance
(SEER, 1988–2008)



TREATMENT

1- Active Surveillance

2- **Focal Therapy** (radiofrequency ablation,

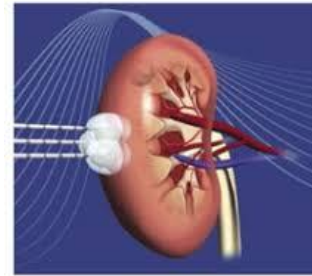
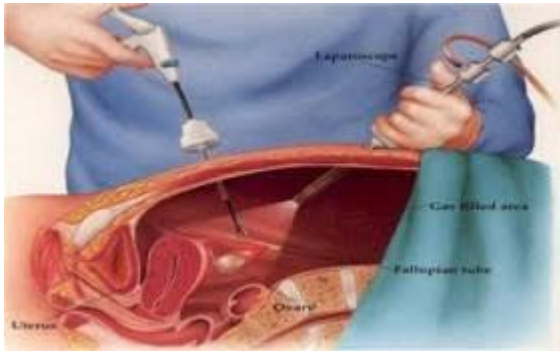
cryoablation, microwave ablation, stereotatic body radiotherapy)

3- **Surgery** (Radical Nephrectomy, Nephron sparing surgery)

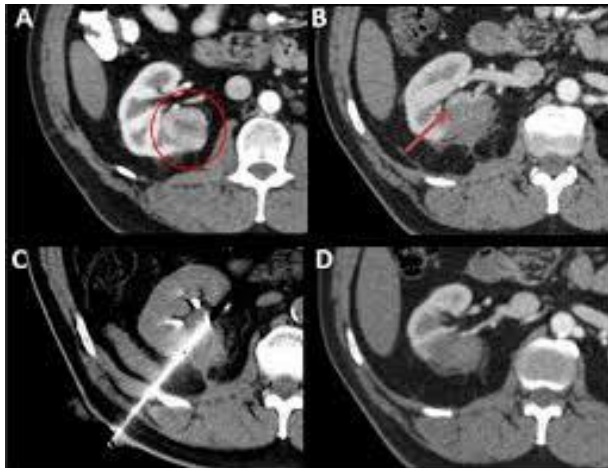
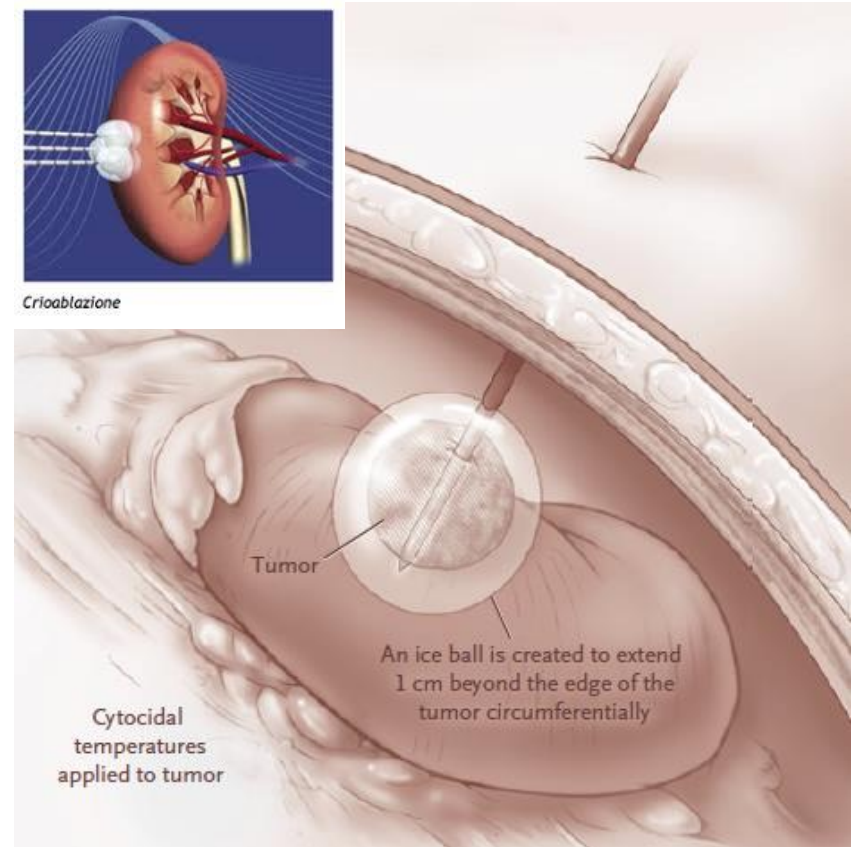
OPEN, LAPAROSCOPIC, ROBOTIC

CRYOABLATION

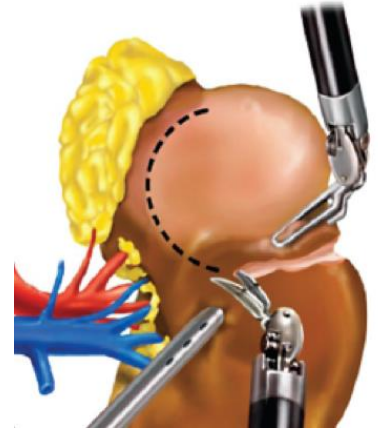
Laparoscopic - Percutaneous



Crioblazione



Nephron Sparing Surgery



When

How

Why

TREATMENT

1- Active Surveillance

2- Focal Therapy (radiofrequency ablation,

cryoablation, microwave ablation, stereotatic body radiotherapy)

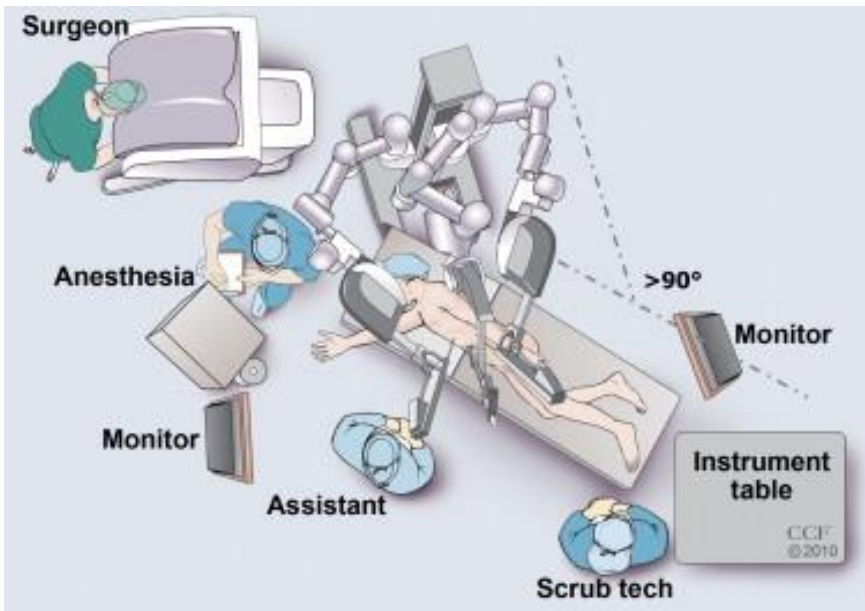
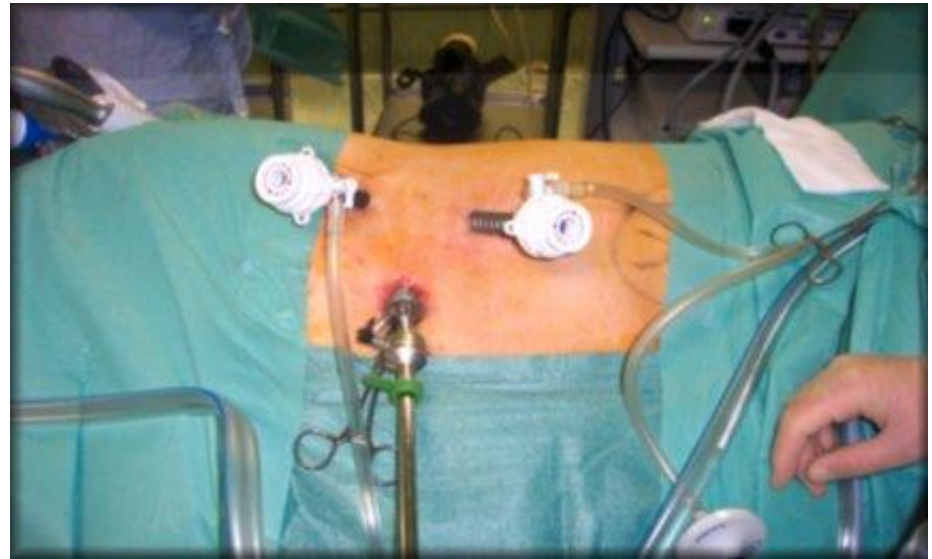
3- **Surgery** (Radical Nephrectomy, Nephron sparing surgery)

OPEN, LAPAROSCOPIC, ROBOTIC

OPEN



LAP



ROBOTIC

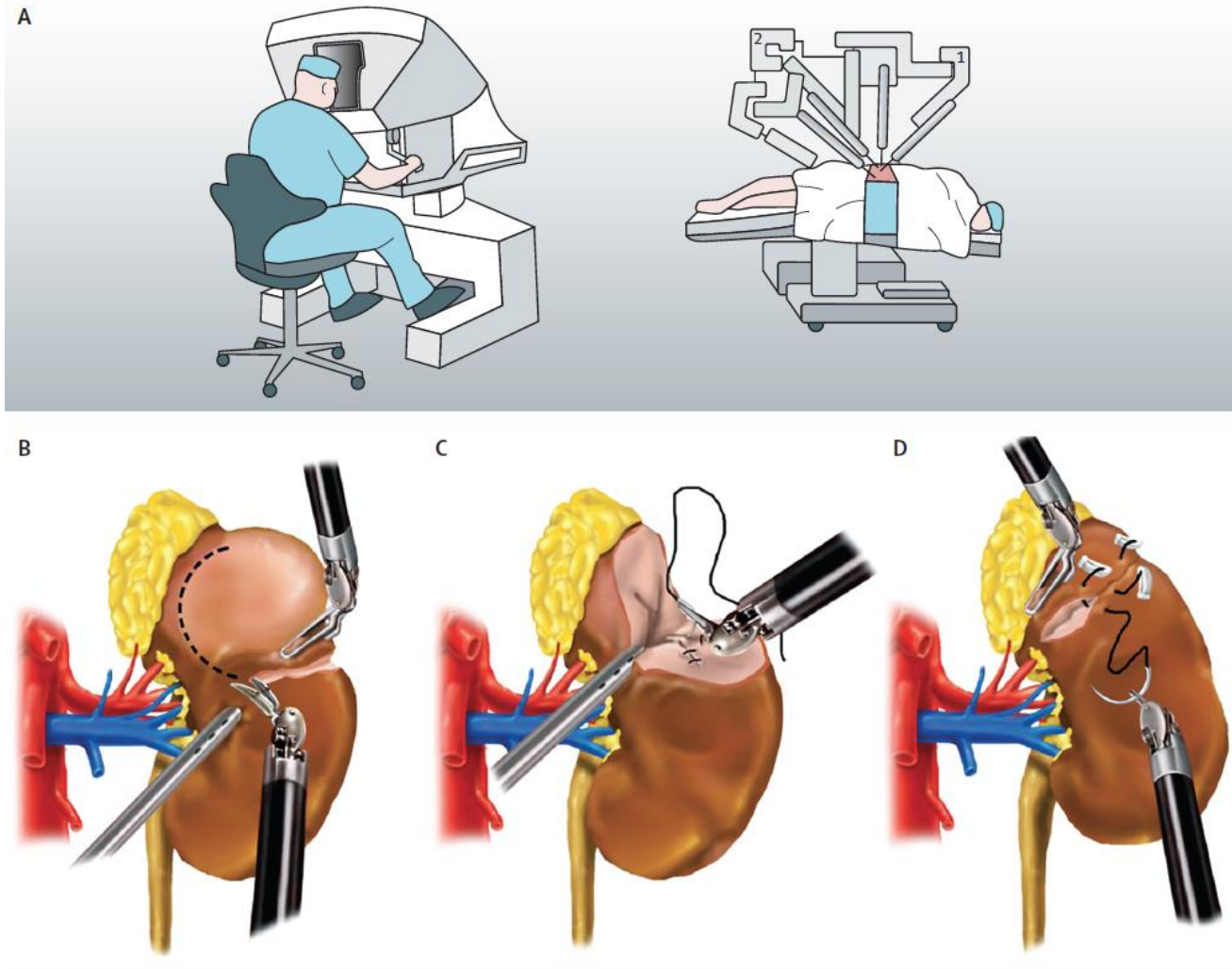
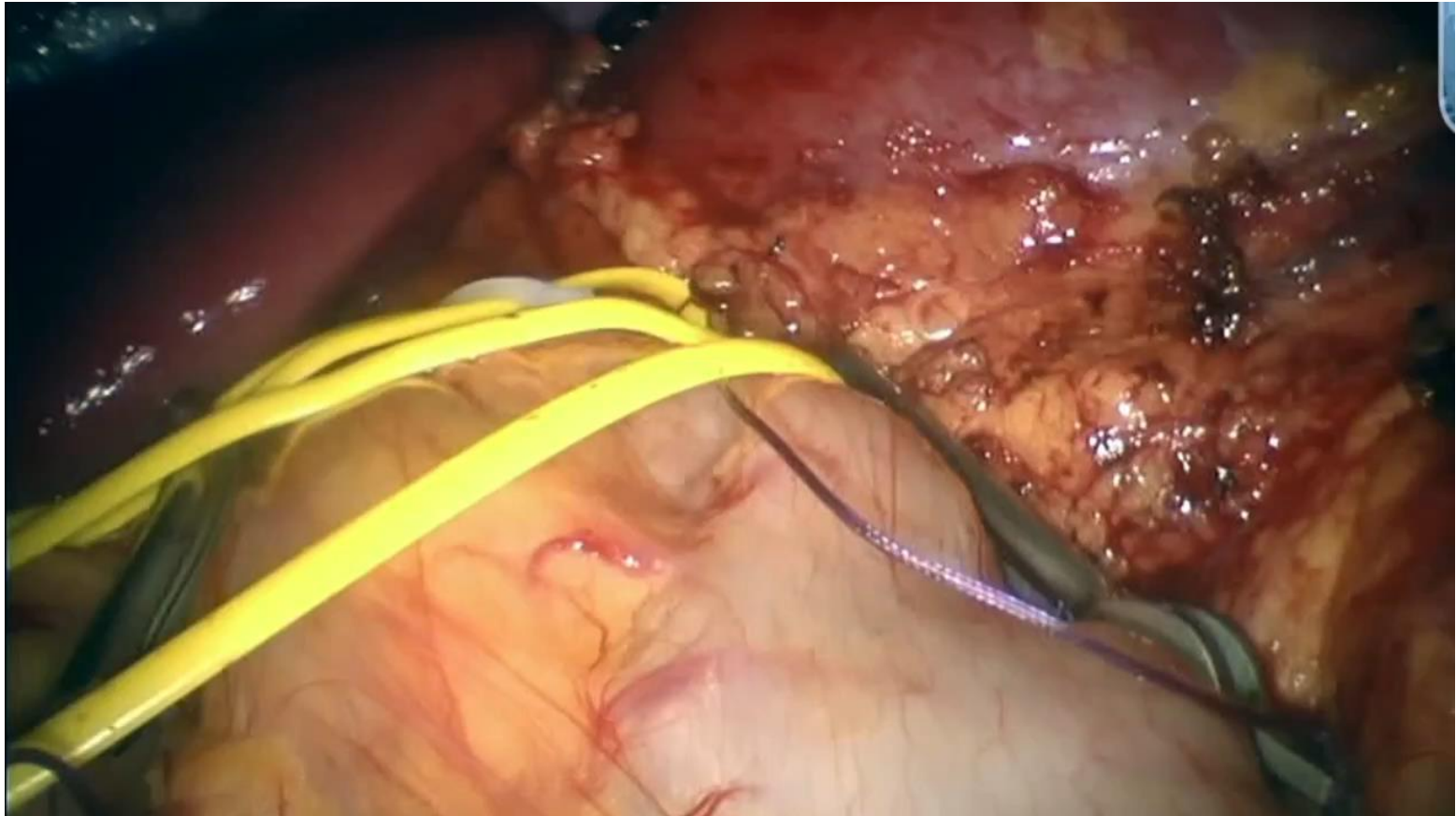


Figure 1: Procedures in robot-assisted nephron-sparing surgery to remove renal cell carcinoma

(A) In robot-assisted surgery, instead of directly moving the instruments, the surgeon performs the normal movements associated with the surgery, and the robotic arms make those movements and use end-effectors and manipulators to perform the actual surgery on the patient. One arm is dedicated to the laparoscope and the two others hold forceps, monopolar curved scissors, a cautery hook, and a large needle driver. The patient is positioned in a modified flank position. Port configuration can vary based on tumour location to optimise the working angles. Surgical excision of the tumour is done by (B) kidney mobilisation, (C) tumour resection (with or without a rim of normal parenchyma according to anatomical and tumour features), and (D) final reconstruction (renorrhaphy).

Robot-assisted partial nephrectomy



Surgical management of kidney cancer

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

2b

The real life: 'Overuse' of radical nephrectomy!

**Community
hospitals**

65000 RCC cases diagnosed in 2012

60% of those were small renal masses

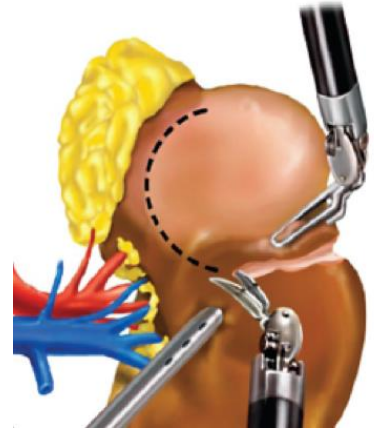
39000 PN candidates

49% treated with PN

**Tertiary care
center**

90% treated with PN
(MSKCC, 2007)

Nephron Sparing Surgery



When

How

Why

COMPARISON OF PN AND RN - RENAL FUNCTION

Secondary analysis of EORTC 30904 trial evaluating renal function

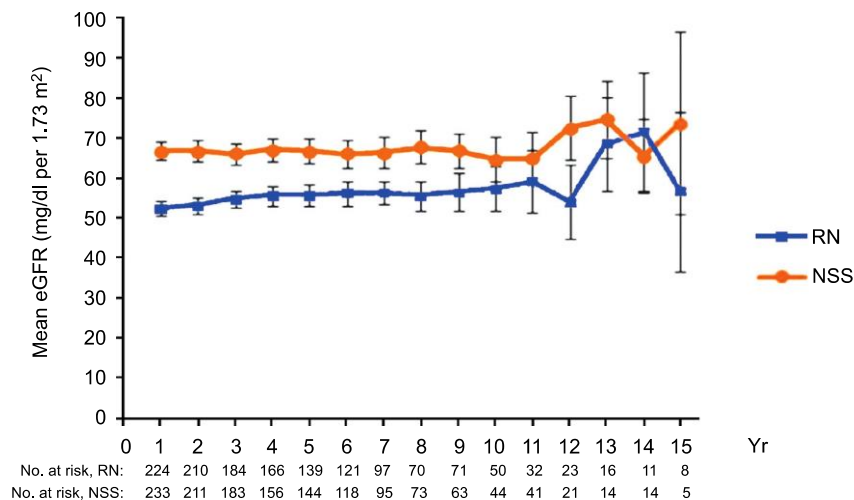
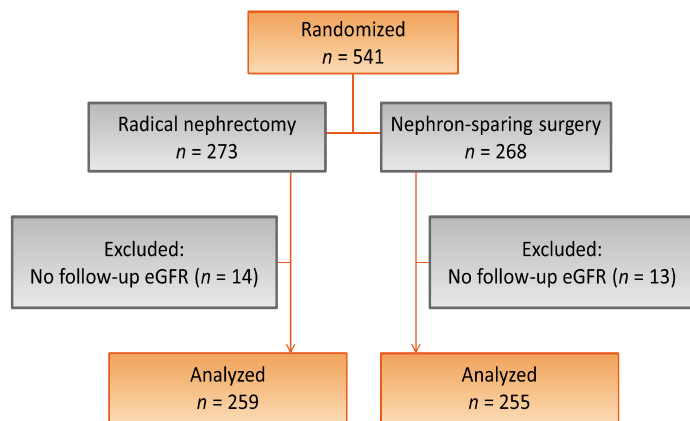


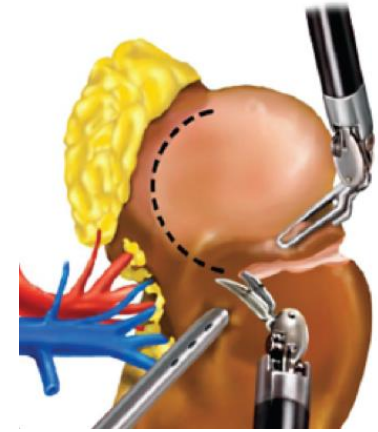
Table 2 – Analysis of lowest estimated glomerular filtration rate (eGFR) and last eGFR according to specified binary cut-offs, by assigned treatment (median follow-up 6.7 yr)

eGFR	Outcome	RN (n = 259)		NSS (n = 255)		Difference, %	95% CI	p*
		No.	%	No.	%			
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.

Potential benefit of Nephron Sparing Surgery



available at www.sciencedirect.com
journal homepage: www.europeanurology.com



Platinum Priority – Kidney Cancer
Editorial by XXX on pp. x–y of this issue

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

U
A
F
N
Decrease te risk of **Cardiovascular Event** relative to radical nephrectomy

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

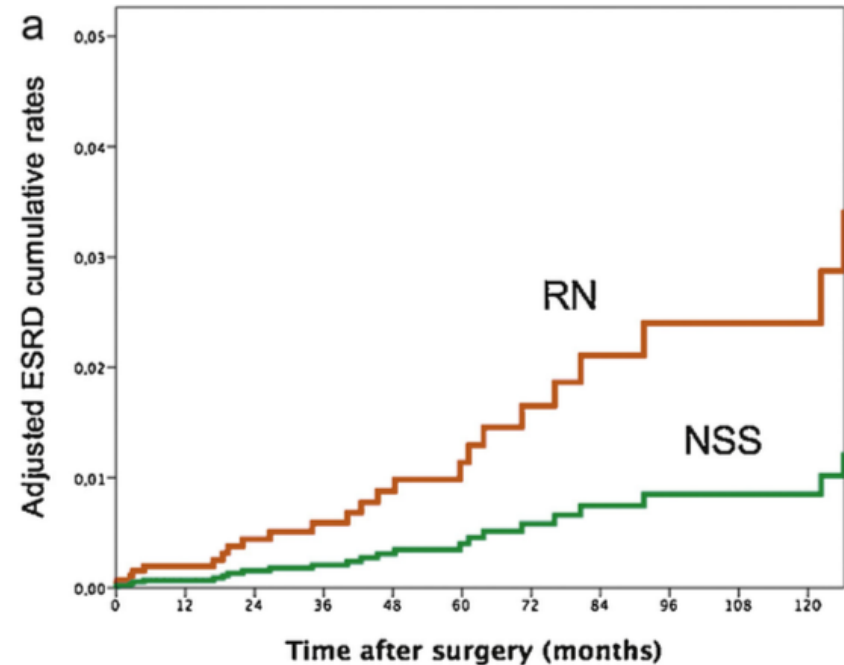


Platinum Priority – Brief Correspondence
Editorial by XXX on pp. x–y of this issue

End-Stage Renal Disease After Renal Surgery in Patients with Normal Preoperative Kidney Function: Balancing Surgical Strategy and Individual Disorders at Baseline

Umberto Capitanio^{a,b,*}, Alessandro Larcher^{a,b}, Carlo Terrone^c, Alessandro Antonelli^d

Decrease te risk of **End Stage Renal Disease**

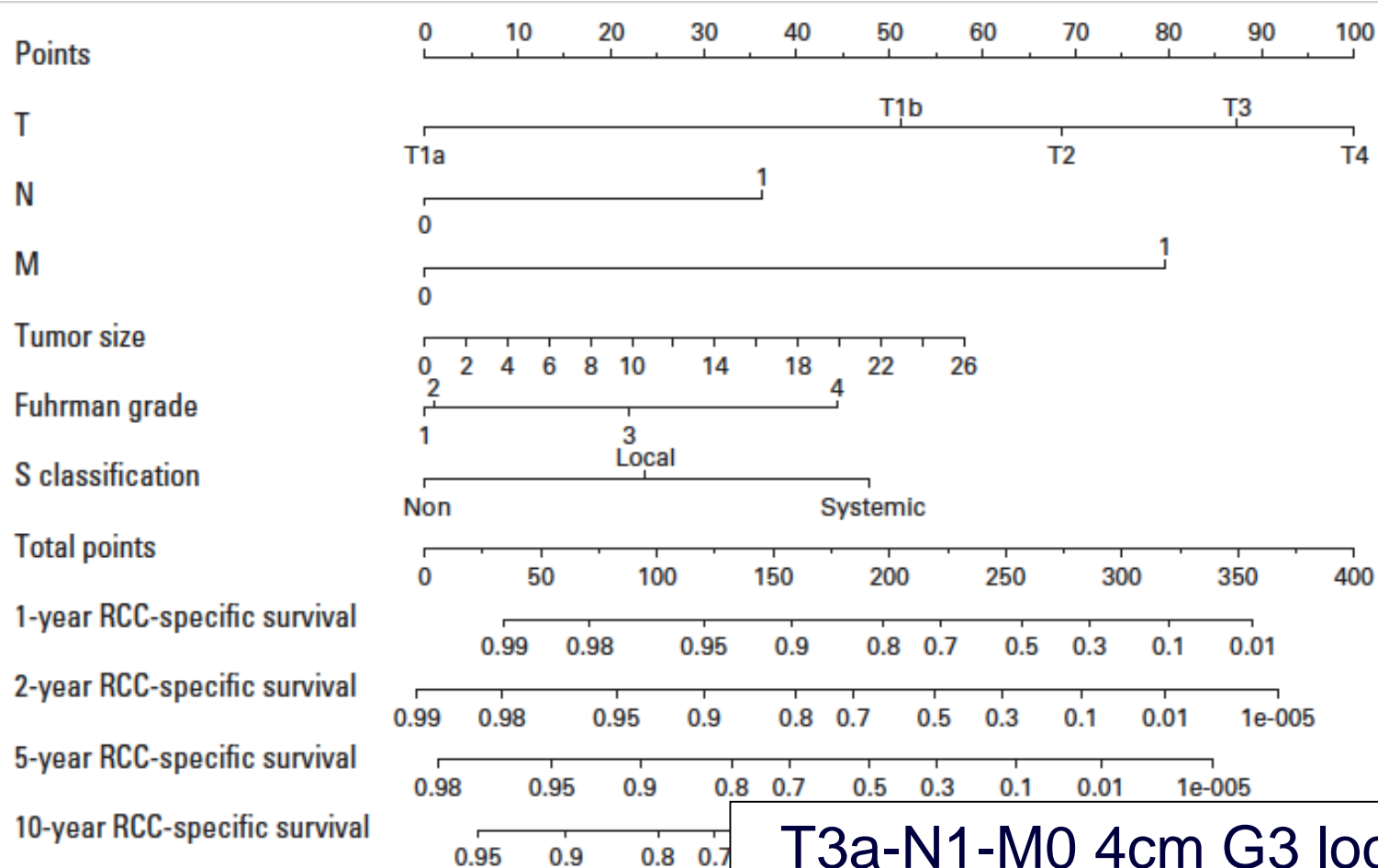


Capitanio U. et al. Eur Urol 2014
Capitanio U. et al. Eur Urol 2016

RENAL CELL CARCINOMA TREATMENT

- LOCALISED DISEASE (T1-T2)
- **LOCALLY ADVANCED DISEASE (T3-T4)**
- METASTATIC (M+)

LOCALLY ADVANCED: PROGNOSIS



T3a-N1-M0 4cm G3 local sympt
CSS 55% at 5-yrs 35% at 10-yrs

THE RESULTS OF RADICAL NEPHRECTOMY FOR RENAL CELL CARCINOMA

CHARLES J. ROBSON, BERNARD M. CHURCHILL AND WILLIAM ANDERSON

*From the Division of Urology, Departments of Surgery and Pathology,
University of Toronto, Ontario, Canada*

(Reprinted from J. Urol, 101: 297-301, 1969)

Radical nephrectomy (according to Robson C et al, 1969):

- Kidney
- Perinephric fat and Gerota
- Ipsilateral adrenal gland
- Retroperitoneal lymph nodes



Charles J. Robson

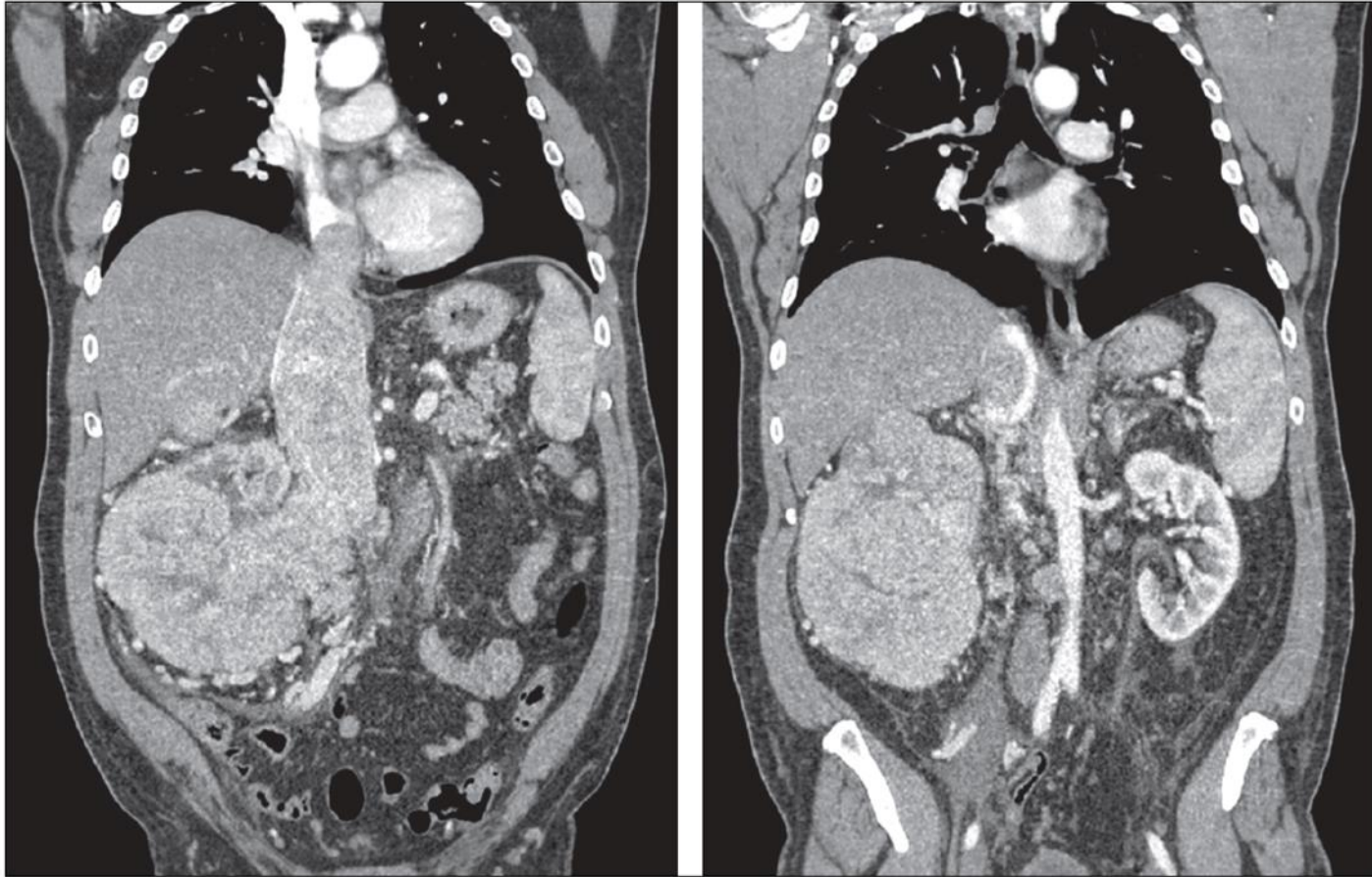
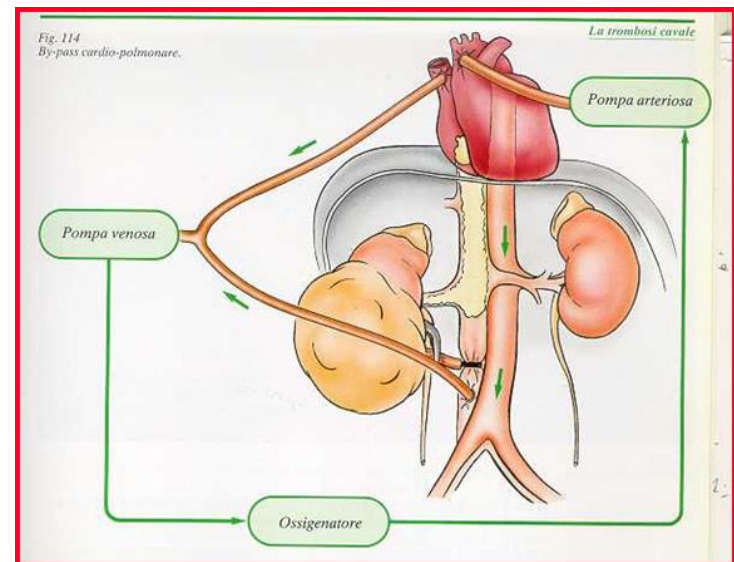
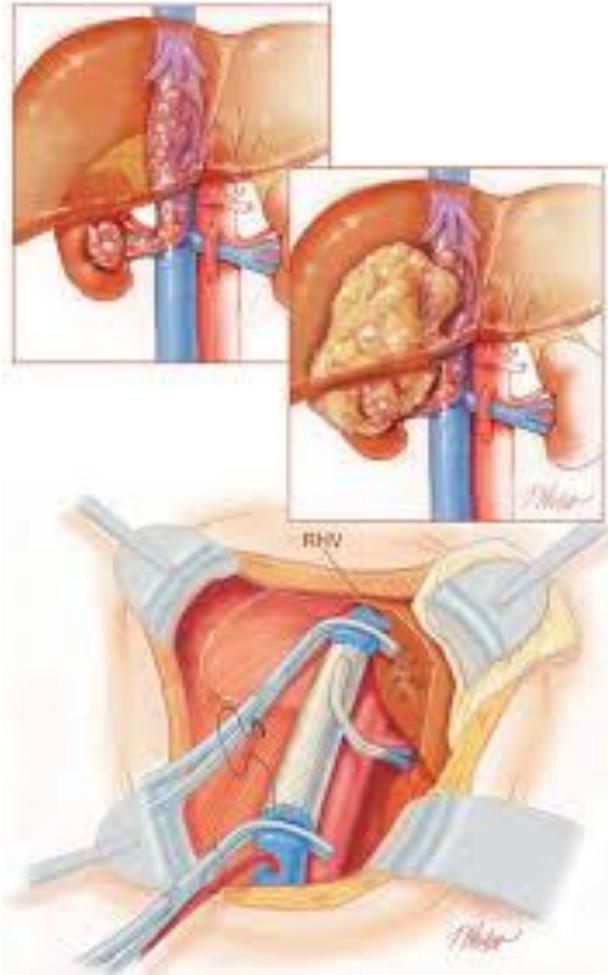


Figure 2: CT scan of a patient aged 55 years with a bulky right kidney tumour and caval thrombus invading the right atrium

Images were taken before nephrectomy and venous thrombectomy, and are two slices from the same scan. Initial presentation was a newly diagnosed right varicocele, followed by fatigue and dyspnoea. The right varicocele was secondary to a venous thrombus occluding the vena cava and its branch, the right spermatic vein. Fatigue and dyspnoea were secondary to initial heart failure and abnormal production of prostaglandins, cytokines, and inflammatory mediators by the tumour.

Caval thrombosis surgery



ROLE OF LYMPHADENECTOMY

LNI rates

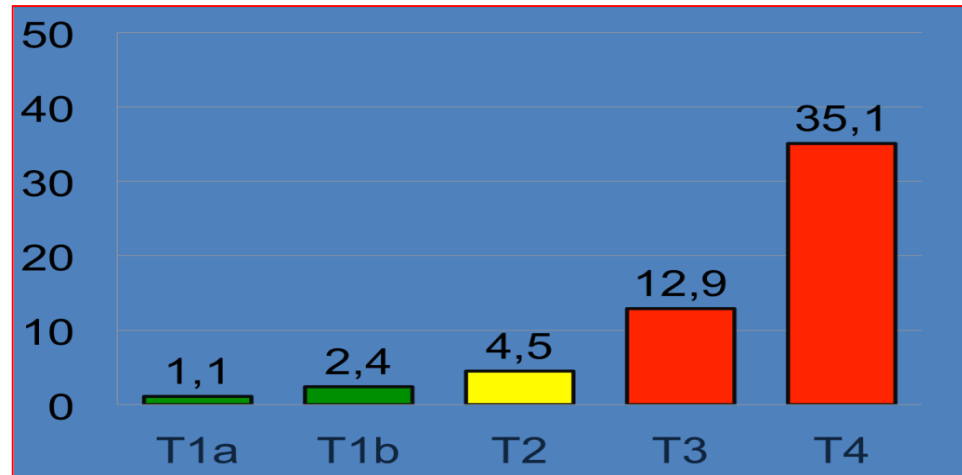


Table 2 – Pathologic N1 prevalence within clinical, surgical, and pathologic features proposed as predictors of regional lymph node involvement at nephrectomy*

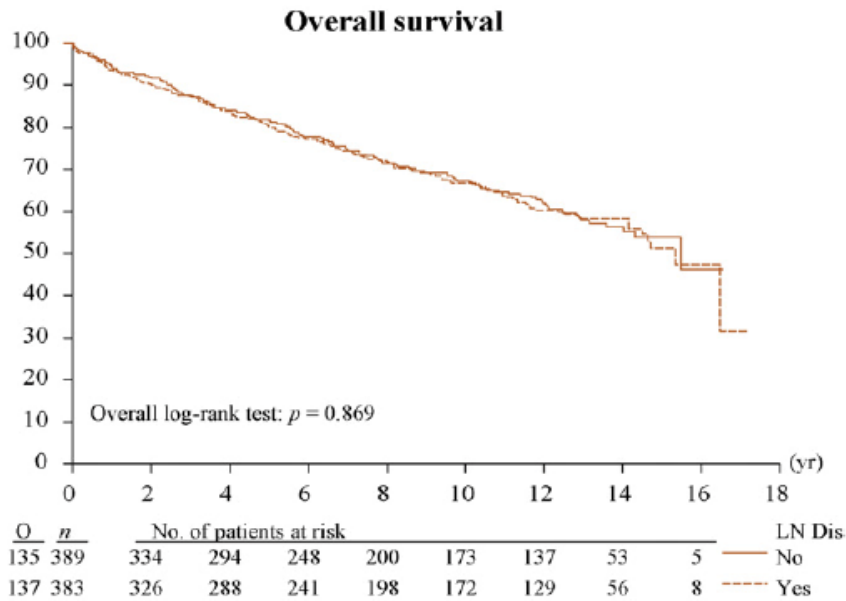
Variable	Blute et al. [31]	Capitanio et al. [28]	Pantuck et al. [6]	Whitson et al. [44]
pT				
1	2.3	1.1	2.4	5.1
2	3.6	4.5	11.4	11.1
3–4	37.1	12.3	30.6	31.0
Fuhrman grade				
I–II	0.6	NA	6.3	7.2
III–IV	8.8	NA	26.0	30.8
Symptomatic at presentation	5.2	NA	NA	NA
Tumor thrombus	8.8	NA	NA	NA
Coagulative tumor necrosis	11.1	NA	NA	NA
Sarcomatoid component	27.5	NA	32.3	NA

NA = not applicable.

* Only series published in the last decade were considered.

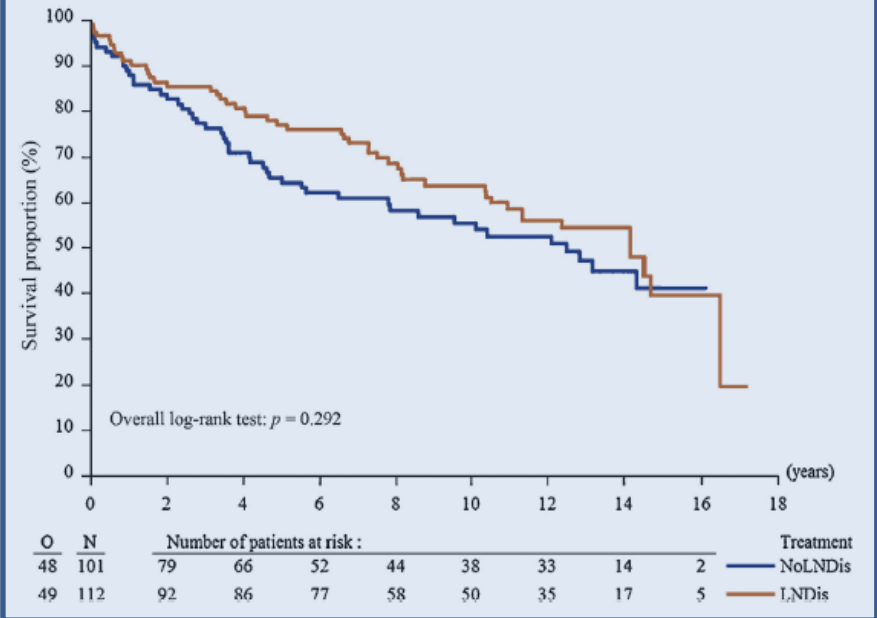
Original EORTC RCT

n=772 cT1-3 N0 M0



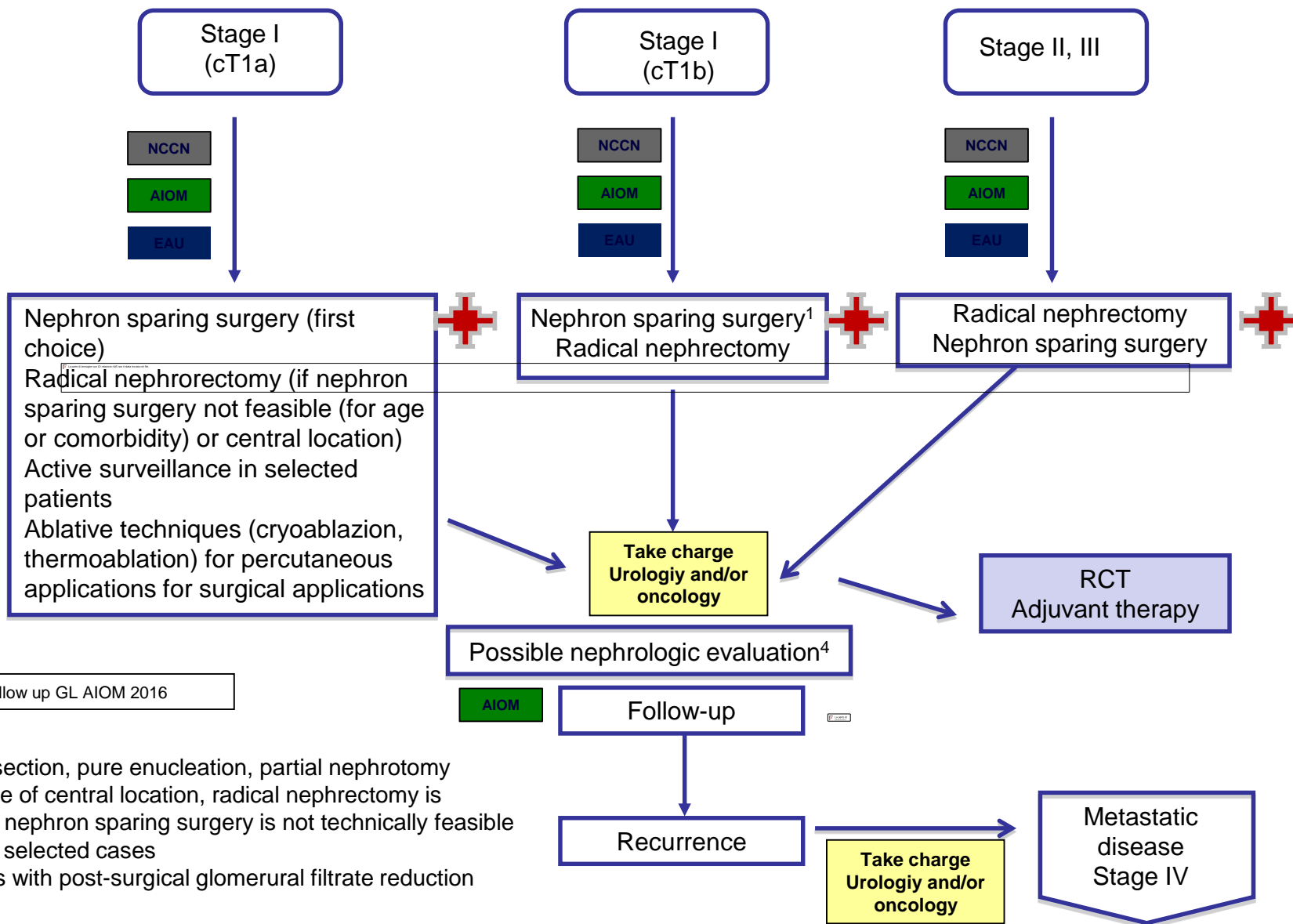
Sub-analysis

n=213 cT3 N0 M0



Overall survival (in years) for cT3 with and without lymph node dissection (subgroup analysis of Blom et al. NoLNDis = radical nephrectomy without lymph node dissection; LNDis = radical nephrectomy with lymph node dissection; O = observed events; N = number at baseline.

Localised or locally advanced renal masses



All. 2: Follow up GL AIOM 2016

- 1Enucleoresection, pure enucleation, partial nephrotomy
- 2In the case of central location, radical nephrectomy is indicated if nephron sparing surgery is not technically feasible
- Stage II, in selected cases
- 4in patients with post-surgical glomerular filtrate reduction

RENAL CELL CARCINOMA PROGNOSTIC FACTORS

✓ Histopatological stage

Bad prognosis in T₃ or N+

✓ Tumor diameter

Bad prognosis if > 10 cm

✓ Cytological grading

Bad prognosis in G3 by OMS,
G3-G4 by Furham

✓ Histological subtype

Bad prognosis in

- ✓ Sarcomatoid
- ✓ Papillary type II

✓ Performance status

RENAL CELL CARCINOMA

PROGNOSTIC FACTORS T N0-M0

Approximately 40% dies from disease progression.

5 years prognosis by **PATOLOGICAL STAGE:**

✓ T₁-T₂ N0-M0: 75-95%

✓ T_{3a} N0-M0: 65-80%

✓ T_{3b} N0-M0: 40-60%

✓ N⁺: 10-20%

✓ M⁺: 0-5%

RENAL CELL CARCINOMA TREATMENT

- LOCALISED DISEASE (T1-T2)
- LOCALLY ADVANCED DISEASE (T3-T4)
- METASTATIC (M+)
 - ✓ At diagnosis
 - ✓ After primary treatment

RENAL CELL CARCINOMA METASTATIC STAGE

Approximately 40% dies from disease progression.

5 years prognosis by **PATOLOGICAL STAGE:**

✓ T₁-T₂ N0-M0: 75-95%

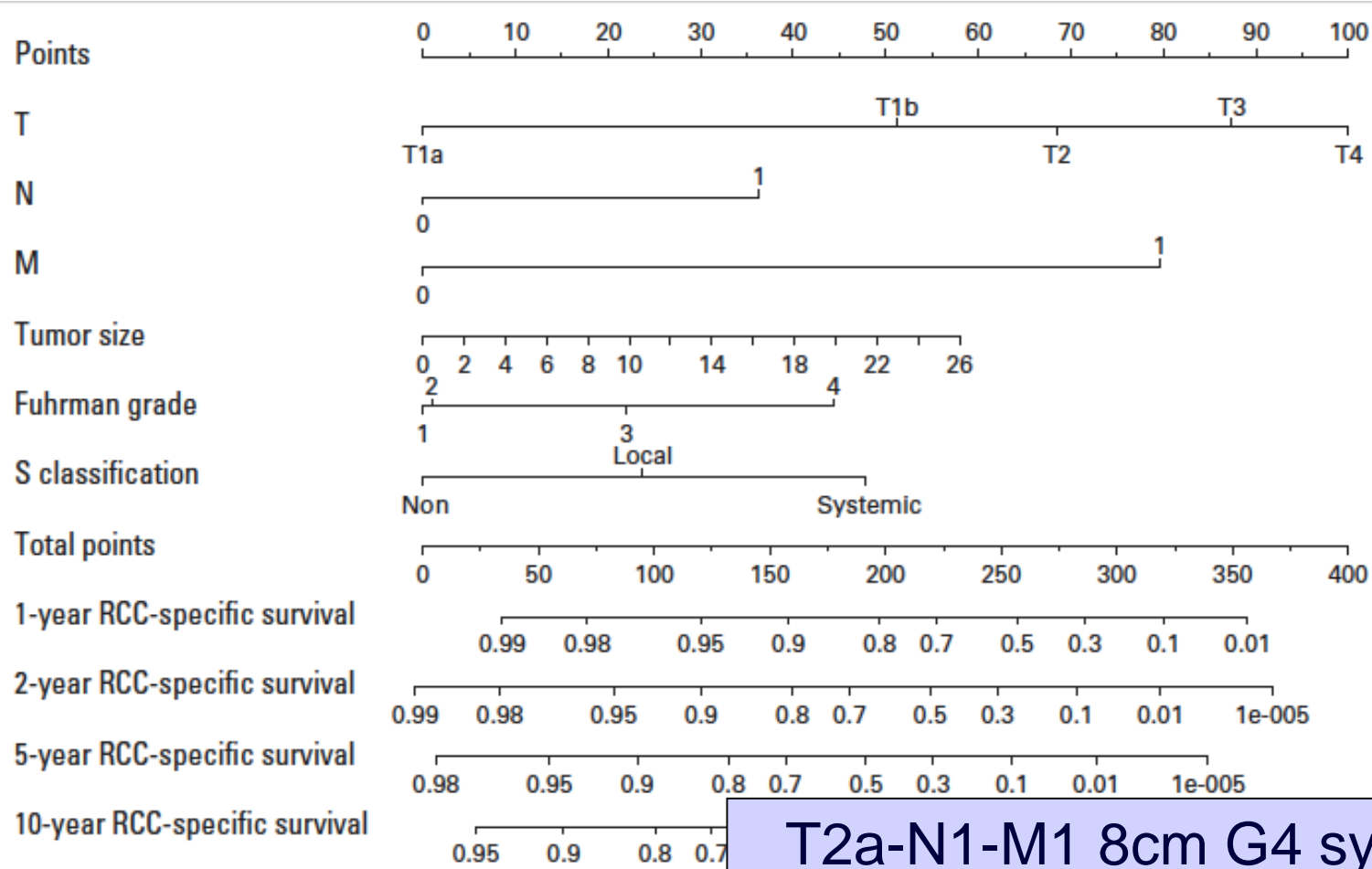
✓ T_{3a} N0-M0: 65-80%

✓ T_{3b} N0-M0: 40-60%

✓ N⁺: 10-20%

✓ M⁺: 0-5%

METASTATIC: PROGNOSIS -NOMOGRAMMA



T2a-N1-M1 8cm G4 syst sympt
 CSS 10% at 1-yrs 2% at 2-yrs

RENAL CELL CARCINOMA

MOLECULAR BIOLOGY

Renal carcinoma is resistant to all currently available chemotherapeutic agents

MDR1 GENE (Multi Drug Resistance)

Encode membrane glycoprotein P-170

It works as a pump for the elimination of the various chemotherapeutic agents structurally not similar to each other

RENAL CELL CARCINOMA

MEDICAL THERAPY

CHEMOTHERAPY

RADIATION THERAPY



NO

RENAL CELL CARCINOMA METASTATIC STAGE

Cyto-reductive nephrectomy
+
Metastasis surgery

For many years it has been the
standard of treatment

New therapies for renal carcinoma

Targeted Therapy

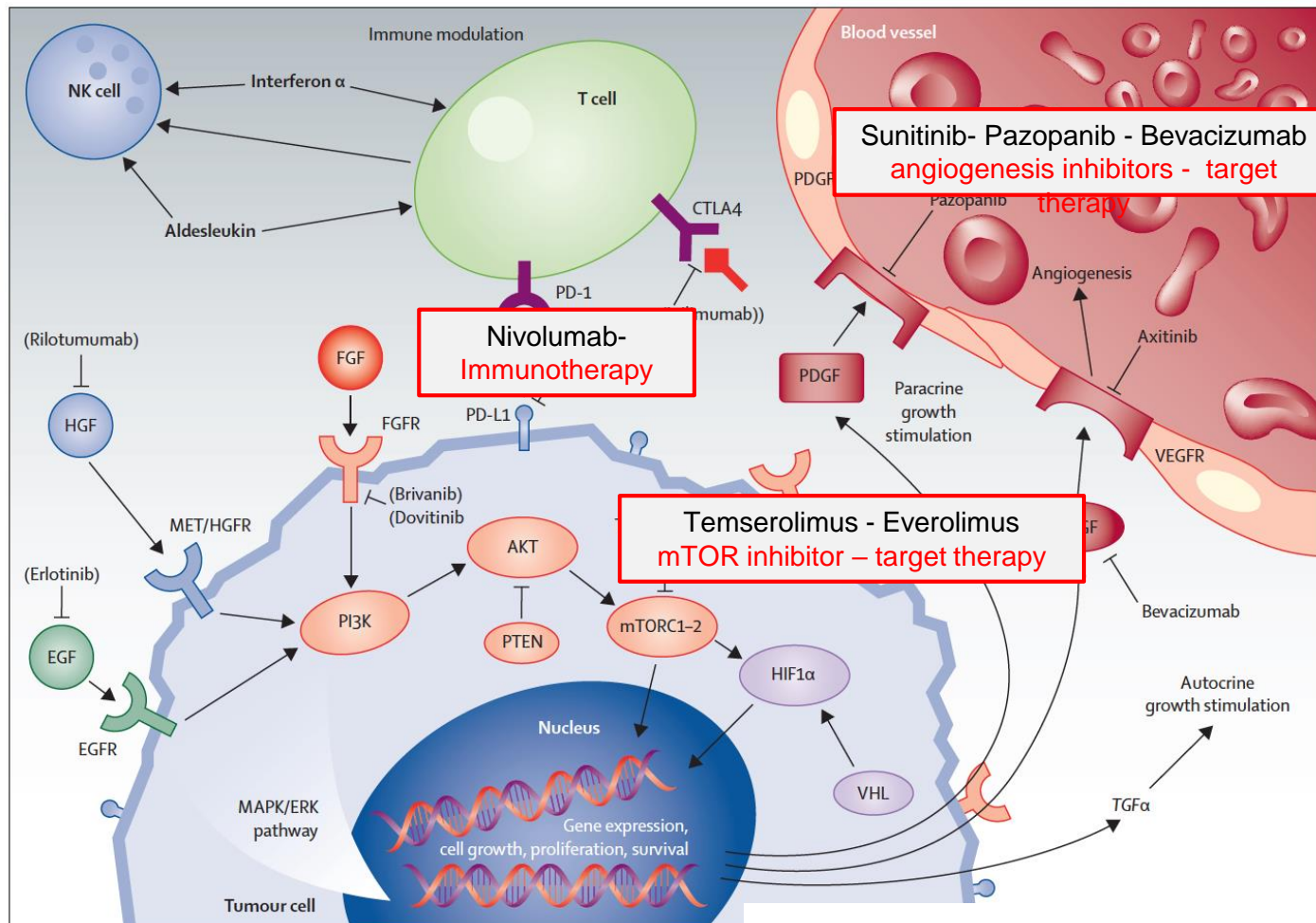


Figure 3: Biological pathways related to development of renal cell carcinoma and treatment. NK=natural killer.

mTOR: protein kinase that regulates cell synthesis

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

AUGUST 2, 2018

VOL. 379 NO. 5

Sunitinib Alone or after Nephrectomy in Metastatic Renal-Cell Carcinoma

A. Méjean, A. Ravaud, S. Thezenas, S. Colas, J.-B. Beauval, K. Bensalah, L. Geoffrois, A. Thiery-Vuillemin, L. Cormier, H. Lang, L. Guy, G. Gravis, F. Rolland, C. Linassier, E. Lechevallier, C. Beisland, M. Aitchison, S. Oudard, J.-J. Patard, C. Theodore, C. Chevreau, B. Laguerre, J. Hubert, M. Gross-Goupil, J.-C. Bernhard, L. Albiges, M.-O. Timsit, T. Lebret, and B. Escudier

A Overall Survival

B Progression-free Survival

Cyto-reductive nephrectomy not always indicated
EAU guidelines

No. at Risk									
Nephrectomy+ sunitinib	226	110	61	40	19	11	4	1	0
Sunitinib alone	224	128	76	44	26	8	3	1	0

No. at Risk									
Nephrectomy+ sunitinib	226	59	10	6	2	1	0		
Sunitinib alone	224	74	28	9	6	2	0		

The Role of Cyto-Reductive Nephrectomy in the era of target therapy

VOLUME 34 · NUMBER 27 · SEPTEMBER 20, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Survival Analyses of Patients With Metastatic Renal Cancer Treated With Targeted Therapy With or Without Cytoreductive Nephrectomy: A National Cancer Data Base Study

Nawar Hanna, Maxine Sun, Christian P. Meyer, Paul L. Nguyen, Sumanta K. Pal, Steven L. Chang, Guillermo de Velasco, Quoc-Dien Trinh, and Toni K. Choueiri

Multivariable HR, 0.45;
95% CI, 0.40 to 0.50; $p < 0.001$

Only 35% underwent CN

- ✓ Younger
- ✓ privately insured
- ✓ academic center
- ✓ lower cT and cN stage

15,390 mRCC treated with targeted therapy, TT (2006-2013)

Hanna et al. JCO 2016

Motzer risk factors: M+ disease

Table 7.1: The Metastatic Renal Cancer Database Consortium (IMDC) risk model [364]

Risk factors**	Cut-off point used
Karnofsky performance status	< 80%
Time from diagnosis to treatment	< 12 months
Haemoglobin	< Lower limit of laboratory reference range
Corrected serum calcium	> 10.0 mg/dL (2.4 mmol/L)
Absolute neutrophil count (neutrophilia)	> upper limit of normal
Platelets (thrombocytosis)	> upper limit of normal

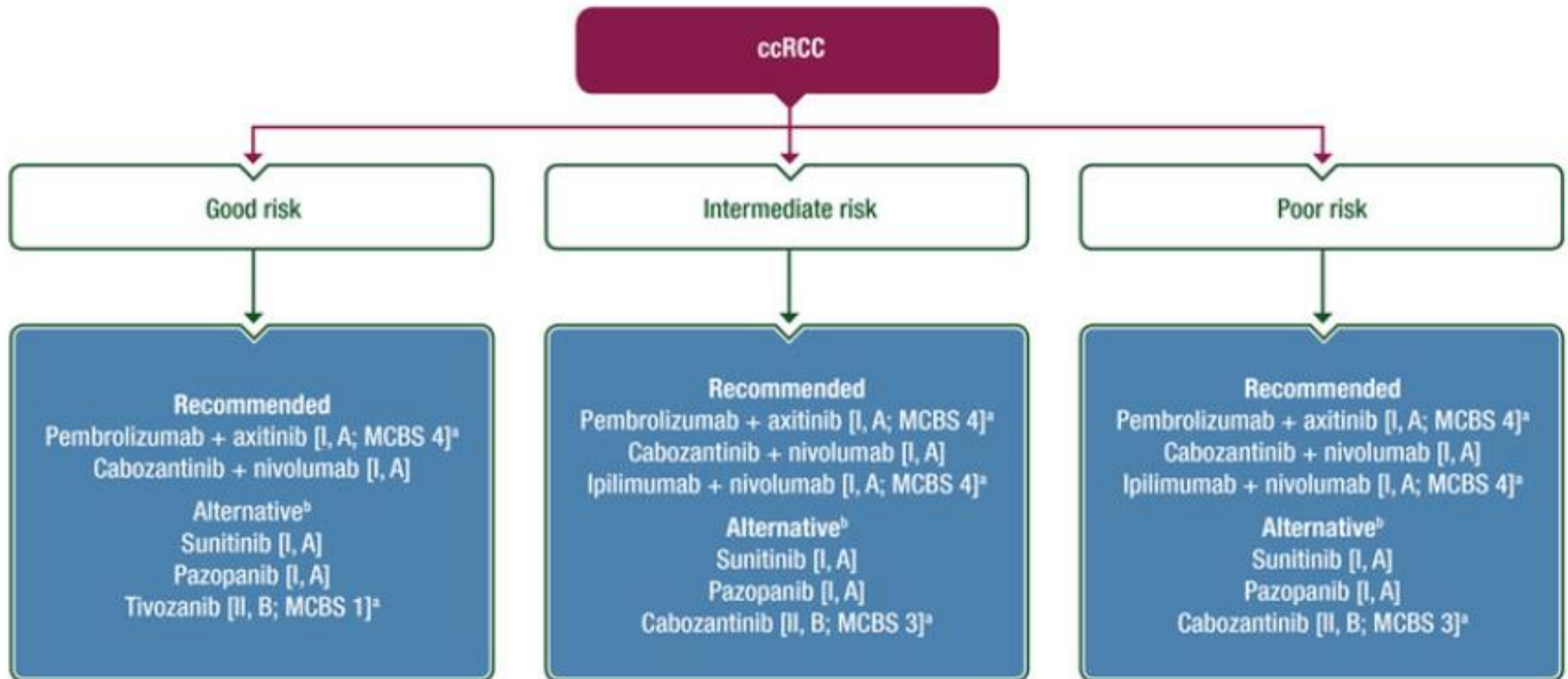
* The MSKCC (Motzer) criteria are also widely used in this setting [357].

** Favourable (low) risk, no risk factors; intermediate risk, one or two risk factors; poor (high) risk, three to six risk factors.

Metastatic disease

- ✓ Low risk: no factors
- ✓ Intermediated risk: 1-2 factors
- ✓ High risk: 3-6 factors

MEDICAL THERAPY



Metastatic renal carcinoma prognosis

in the target therapy era

Table 7.2: Median OS and percentage of patients surviving two years treated in the era of targeted therapy per IMDC risk group (based on references [391, 407])

IMDC Model	Patients**		Median OS* (months)	2-y OS (95% CI)**
	n	%		
Favourable	157	18	43.2	75% (65-82%)
Intermediate	440	52	22.5	53% (46-59%)
Poor	252	30	7.8	7% (2-16%)

* Based on [407]; ** based on [391]

CI = confidence interval; IMDC = Metastatic Renal Cancer Database Consortium; n = number of patients; OS = overall survival.

EAU guidelines 2020

UPPER URINARY TRACT TUMORS

EPIDEMIOLOGY

- ✓ They are relatively rare: 10% of all renal cancers.
- ✓ Male/female ratio: 3/1
- ✓ 5% of all urothelial tumors
- ✓ 2-4% of patients with bladder cancer

AETIOLOGY

- ✓ Cigarette smoke
- ✓ Abuse of analgesics (Fencetine)
- ✓ Cyclophosphamide
- ✓ Industrial dyes

UPPER URINARY TRACT TUMORS

Histhology

- **Urotelial cancer: 90%**
- **Squamocellular carcinoma: 7-9%**
- **Adenocarcinoma: 1%**

UPPER URINARY TRACT TUMORS

Symptoms

- **Gross haematuria : 75%**
 - **Flank pain : 30%**

Deep and continuous pain (gradual obstruction and relaxation of the excretion pathway)

Acute renal colic pain (passage of clots along the ureter)

UPPER URINARY TRACT TUMORS

Diagnosis

UROGRAPHY:

- ✓ Defect of radiopaque filling of the excretion pathway (renal pelvis, calyx, ureter) evident in 75% of these cancers
- ✓ Often not diagnostic because the kidney is functionally excluded



UPPER URINARY TRACT TUMORS

Diagnosis

ABDOMEN CT

- ✓ The preset **gold standard** for **diagnosis** (low sensitivity of ultrasound on the excretic tract) and for **staging**.
- ✓ Useful for the evaluation of possible lymphadenopathies (staging) or infiltrations of adjacent structures.

LEFT RENAL PELVIS TUMOR



UPPER URINARY TRACT TUMORS

Diagnosis

URO-MRI

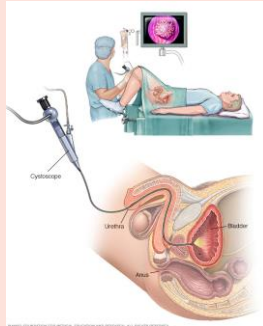
- ✓ Contrast allergy
- ✓ Impaired renal function



UPPER URINARY TRACT TUMORS

Other diagnostic tests

CISTOSCOPY (office procedure)
often associated with bladder cancer

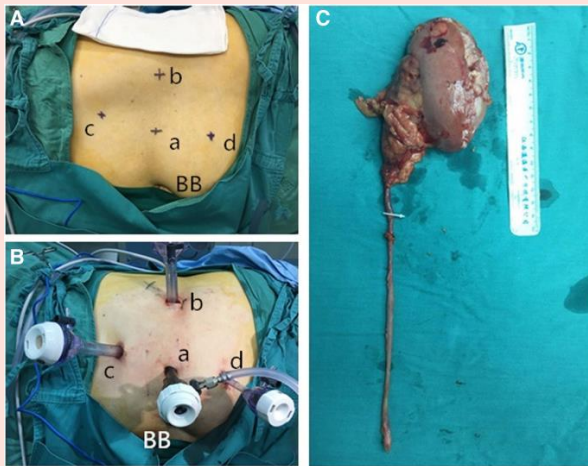


- **URETERORENOSCOPY** (operating room)



UPPER URINARY TRACT TUMORS THERAPY

NEPHROURETERECTOMY with
removal of ureteral meatus
And **LIMPHADENECTOMY**



GOLD STANDARD

**ENDOSCOPIC
LASER ABLATION**



SELECTED CASES

Clinical scenario I

Male 62 y.o.

- ✓ I did an ultrasound examination during a company check-up.
- ✓ They found **a mass in my kidney**.
- ✓ The exam describes it as **anechoic** and with a diameter of 4 cm.
- ✓ Help me! I have a kidney cancer. I need surgery right now!

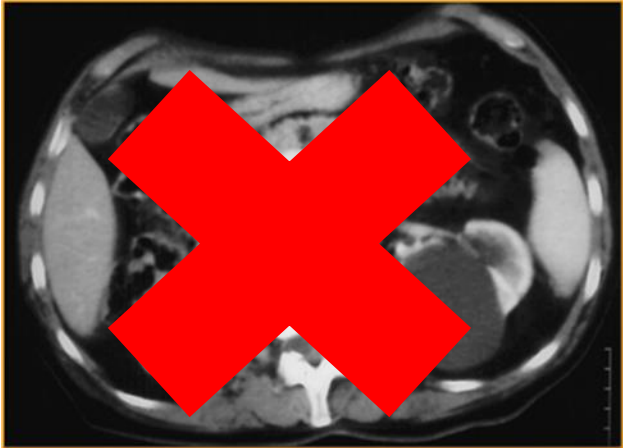
Clinical scenario I



Simple renal cyst



Complex renal



Bosniack
Classification



Clinical scenario II

Male 62 y.o.

- ✓ I saw blood in the urine (**macroscopic haematuria**)
- ✓ I took an antibiotic and it is gone.
- ✓ Nouthin to be worried about , isn't it?

Clinical scenario II

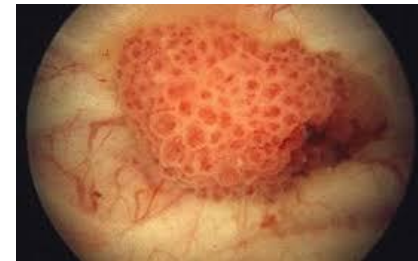
Hematuria has always to be investigated

I level test

- ✓ Urinary tract ultrasound

II level tests:

- ✓ Urinary tract CT
- ✓ Cystoscopy

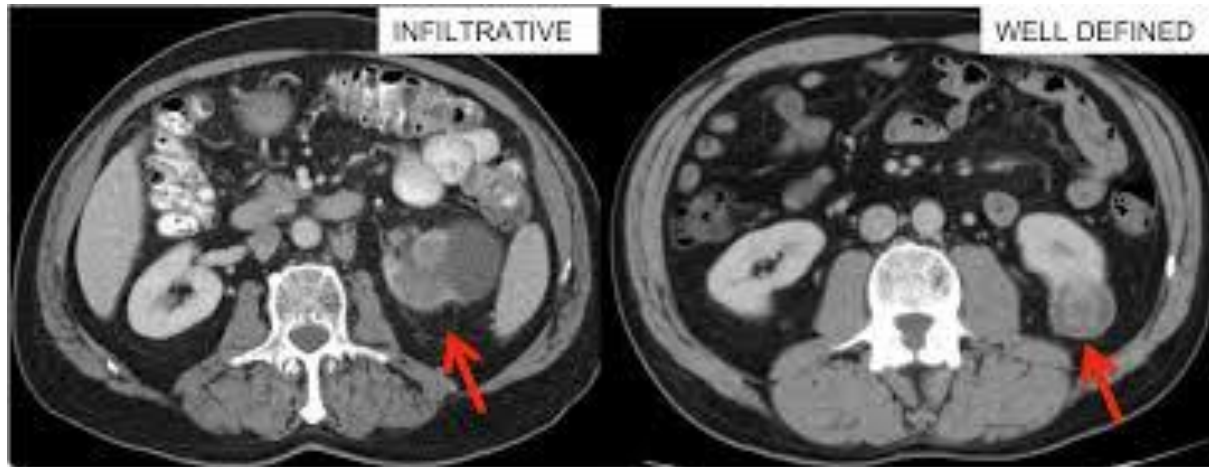


Clinical scenario III

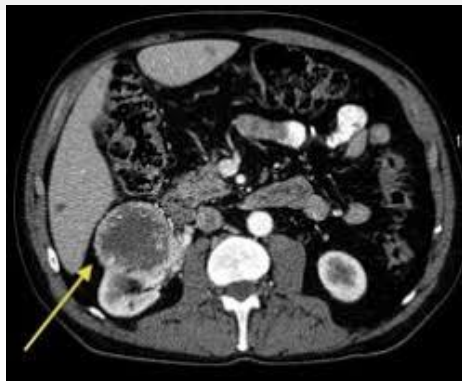
Male 62 y.o.

- ✓ I did an ultrasound examination during a company check-up.
- ✓ They found a **mass in my kidney**.
- ✓ The radiologist describes it as 4 cm in diameter. He told me that it is not a cyst, and recommended an urological consultation to arrange a **biopsy**.
- ✓ Let's do this biopsy right now!

RENAL CELL CARCINOMA CT DIAGNOSIS



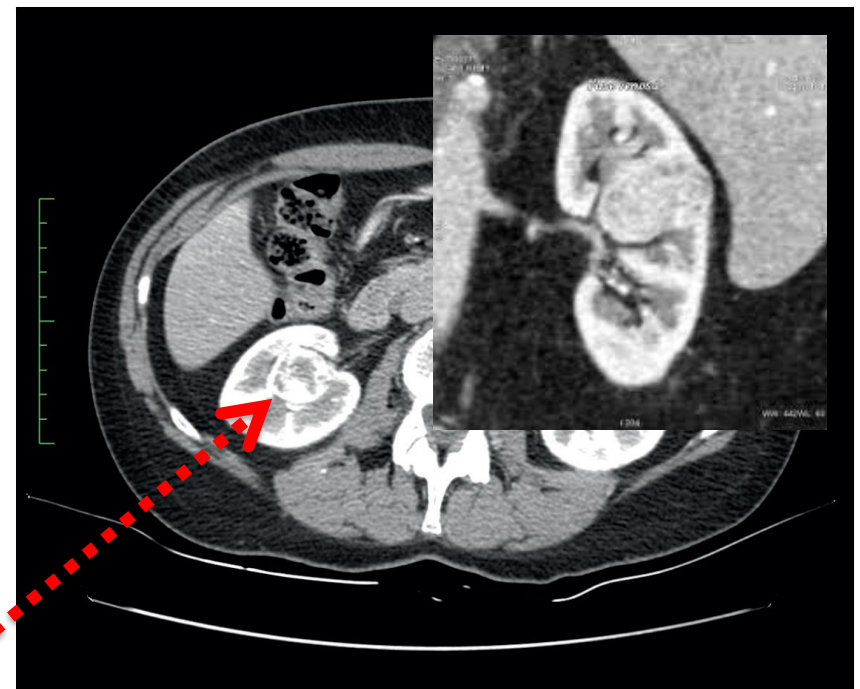
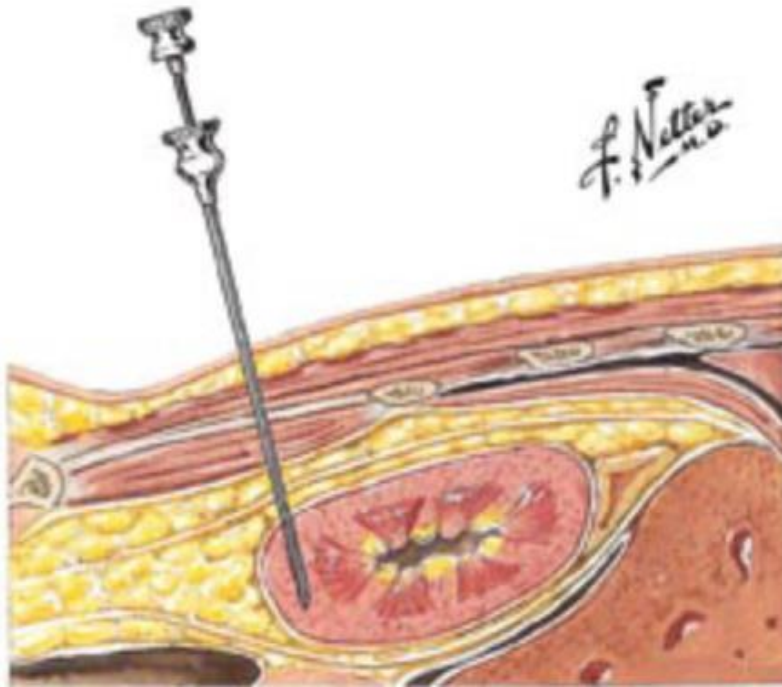
Staging rather than diagnosis
High sensitivity and specificity



Do you always need a kidney biopsy to confirm the diagnosis?

Ecoguided percutaneous biopsy only in special cases

- ✓ Active surveillance
- ✓ Small masses that do not allow conservative surgery



CT scan showing a small (intrarenal) mass of the right kidney. Percutaneous biopsy revealed the presence of renal oncocytoma

Clinical scenario IV

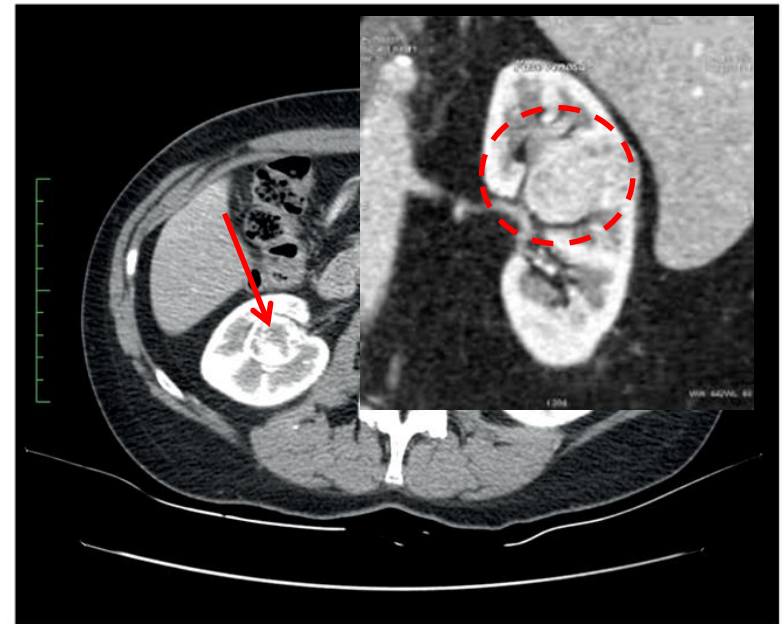
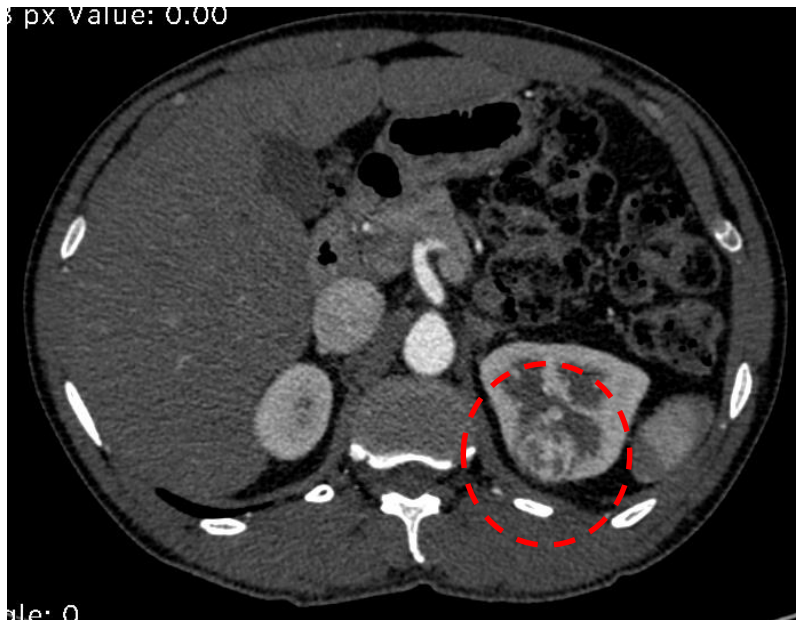
Male 62 y.o.

- ✓ I did an ultrasound examination during a company check-up
- ✓ They found a mass in my kidney
- ✓ The radiologist describes it as 4 cm in diameter. I had a CT scan that confirms it is a renal tumor.
- ✓ Doctor. I you to organize as soon as possible the removal of the entire kidney (**nephrectomy**).

4 cm = T1a

Diameter < 5 cm
Nephron sparing surgery

Nephron Sparing Surgery In which cases?



*CT scan showing a small (intrarenal) mass of the right kidney.
Percutaneous biopsy revealed the presence of renal oncocytoma*