

Renal Cell Carcinoma (RCC)

* Renal parenchyma $\xrightarrow{\text{Embryo}}$ metanephryblasty

* Ureter + Renal pelvis $\rightarrow$ Ureteric bulb
Wolffian duct $\leftarrow$
= mesonephric duct.

المنشأ من الكلى في الجنين
Tumors in management. in presentation

* Main Renal tumor in parenchyma
in Adult $\rightarrow$ RCC = Adenocarcinoma
= hypernephroma
in paediatric $\rightarrow$ Wilms' tumor
= nephroblastoma.

system
Collecting ~~system~~ (from Calyx to Ureter + UP)
 $\downarrow$
Lined by epithelium
 $\downarrow$
Urethral Cancer $\rightarrow$ Squamous Cell Carcinoma
or Carcinoma Cell Carcinoma

management of Urethral Cancer

Urethral Cancer

Upper tract Urethral Cancer
Gold standard management of

Radical nephroureterectomy
+ bladder cuff excision

+ Ureter + kidney (with) ⊗
bladder cuff

Unstable ← (unstable ?? Ureter ??)

Gold management of Wilms T. of
Radical nephroureterectomy

RCC →

Renal tumor

~~1. renal mass~~
1. renal mass

benign

malignant

most Common

RCC → most Common

Simple Cyst

Malignant
T.

GEULU e'usu *

most Common

benign solid mass

Papillary Adenoma

Renal Tumors

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Epidemiology

Renal cell carcinoma represents around 3% of all cancers, with the highest incidence occurring in Western countries.

Generally, during the last two decades until recently, there has been an annual increase of about 2% in incidence both worldwide and in Europe leading to approximately 99,200 new RCC cases and 39,100 kidney cancer-related deaths within the European Union in 2018.

Aetiology

MCCP 1/2 2

Except 1/1

DM 1/2 2

سبب المرض

(Risk factor)

Aetiological factors include lifestyle factors such as smoking, obesity, and hypertension.

In a recent studies also diabetes was found to be detrimental.

Having a first-degree relative with kidney cancer is also associated with an increased risk of RCC.

A number of other factors have been suggested to be associated with higher or lower risk of RCC, including specific dietary habits and occupational exposure to specific carcinogens, but the literature is inconclusive.

Renal cell carcinoma is the most common solid lesion within the kidney and accounts for approximately 90% of all kidney malignancies.

Details

المزيد من التفاصيل

Histological diagnosis

Renal cell carcinomas comprise a broad spectrum of histopathological entities described in the 2016 World Health Organization (WHO) classification.

most common type

(65-85%)

there are three main RCC types: clear cell (ccRCC), papillary (pRCC-type I and II) and chromophobe (chRCC).

The RCC type classification has been confirmed by cytogenetic and genetic analyses.

Histological diagnosis includes, besides RCC type; evaluation of nuclear grade, sarcomatoid features, vascular invasion, tumour necrosis, and invasion of the collecting system and peri-renal fat, pT, or even pN categories.

سبب المرض
Glycoprotein + lipid ← see Cytoplasm

(65-85%)

Clear-cell RCC

- Overall, clear-cell RCC (ccRCC) is well circumscribed and a capsule is usually absent. The cut surface is golden-yellow, often with hemorrhage and necrosis.
- Loss of chromosome 3p and mutation of the von Hippel-Lindau (VHL) gene at chromosome 3p25 are frequently found, including additional tumor suppressor genes including SETD2, BAP1, and PBRM1.



(10-15%)

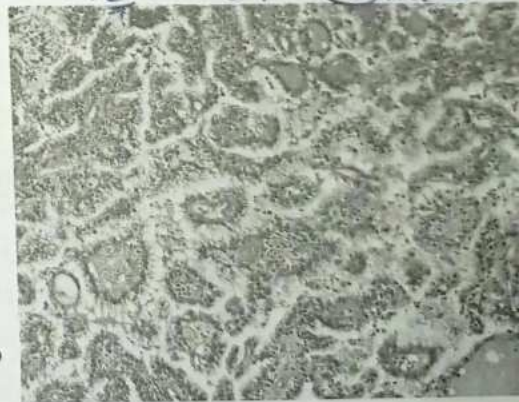
Papillary RCC

End stage Renal disease

is the most common

RCC
Clear cell
~~is the~~
Incidence is
the most common

- Papillary RCC is the second most commonly encountered morphotype of RCC. Papillary RCC has traditionally been subdivided into two types.



(1.5%)

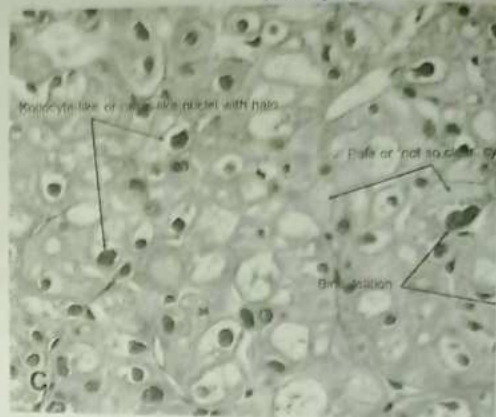
Chromophobe RCC

Renal oncocytoma

100%

Associated with oncocytoma
with another benign tumor

Overall, chRCC is a pale tan, relatively homogenous and tough, well-demarcated mass without a capsule. Chromophobe RCC cannot be graded (by the Fuhrman grading system), because of its innate nuclear atypia.



Other renal tumours

Other renal tumours constitute the remaining renal cortical tumours. These include a variety of uncommon, sporadic, and familial carcinomas, some only recently described, as well as a group of unclassified carcinomas.

(1%)/ Poor survival / (20-30) Young age

Renal medullary carcinoma:

Renal medullary carcinoma (RMC) is a very rare tumor, comprising < 0.5% of all RCCs, predominantly diagnosed in young adults (median age 28 years) with sickle haemoglobinopathies (including sickle cell trait).

Common description: Carcinoma associated with end-stage renal disease; acquired cystic disease-associated RCC

Cystic degenerative changes (acquired cystic kidney disease [ACKD]) and a higher incidence of RCC, are typical features of end-stage renal disease (ESRD).

Renal cell carcinomas of native end-stage kidneys are found in approximately 4% of patients.

benign
tumor

Papillary adenoma: ۲.

+ diagnosed at biopsy
Clinical

Hereditary kidney tumours: .5

Hereditary kidney tumours:
Five to eight percent of RCCs are hereditary; to date there are ten hereditary RCC syndromes associated with specific germline mutations, RCC histology, and comorbidities.

Hereditary RCC syndromes are often suggested by family history, age of onset and presence of other lesions typical for the respective syndromes.

Median age for hereditary RCC is 37 years; 70% of hereditary RCC tumors are found in the lowest decile (< 46 years old) of all RCC tumors.

Hereditary 11 to 12 Colloid
Syndrom

Von Hippel - Lindau

Autosomal dominant disease

extra ←
Urinary
↓
Cerebellar
Hemangioblastoma

~~Urinary~~
Urinary

Gene defect → Short arm
Chromosome (3)

Angiomyolipoma:

Angiomyolipoma (AML) is a benign mesenchymal tumor, which can occur sporadically or as part of tuberous sclerosis complex.

Overall prevalence is 0.44%, with 0.6% in female and 0.3% in male populations.

Only 5% of these patients present with multiple AMLs.

Angiomyolipoma belongs to a family of so-called PEComas (perivascular epithelioid cell tumors), characterized by the proliferation of perivascular epithelioid cells.

Some PEComas can behave aggressively and can even produce distant metastases. Classic AMLs are completely benign

Angiolipoma

parabolic

T. sclerosing Syndrom

benign

 $11:34$

← hereditary RCC 11 = 15% *

present in younger age group

- (+) multiple (multifocal)
- (+) bilateral

(*) sporadic RCC incidence age > 65 y.

1/8 hereditary syndromes 11 = 2.5% *

Temporal sclerosing syndrome

* Autosomal dominant

TSS(1) → chromosome (9)

(2) → = (12)

* Triad 11 = 2.5%

① Adenoma (specious) ??

nasolabial fold ② Mental retardation

③ Seizures

benign Tumor 11 = 25%

Angiomyolipoma

RCC ~ 1/2 *

Temporal
Sclerosing

Ash leaf
spot

Trunk

Skin
manifestation

⊕ Shagreen patches

↓
oral vacuole

Trunk

⊕ periangular fibroma

~~Thyroid~~ the virus sy. ← Syndrome ~ I

Autosomal dominant

(Chromophobe) RCC

oncocytoma ~ benign Tumor

extra urinary presentation
عالب بجا ب

Younger age / Emergency / dysnea

⊕ Spontaneous pneumothorax

Tension

Fatal pneumothorax

presentation of Angiomyolipoma?

usually related to the size

< 4 cm → Asymptomatic

> 4 cm → Variable

bleeding due to blood supply to tumor

Collecting U/s of retro peritoneal hemorrhage

* Management of Angiomyolipoma :

< 4 cm → follow up

> 4 cm



presentation of

→ life threatening bleeding

⊕ hemodynamic instability

response → resuscitation

→ exploration + partial nephrectomy

ل (و + جاب ال Resuscitation ال Fluid

invasive Approach

لعل

ال Vessel ال ال الجزي ال

ضيق

سيفل ال Femoral ال ال Renal ال

A-

A-

ال branch.

Never diagnosed by Radiological
Radical ^{or} partial nephrectomy ← RCC ← + metastasis ← Renal oncology

Renal oncocytoma: .7

Oncocytoma is a benign tumor representing 3-7% of all solid renal tumors and its incidence increases to 18% when tumors < 4 cm are considered.

5) ^{malignant} The diagnostic accuracy of imaging modalities (CT, MRI) in renal oncocytoma is limited and histopathology remains the only reliable diagnostic modality.

Standard treatment for renal oncocytoma is similar to that of other renal tumors; surgical excision by partial- or RN with subsequent histopathological verification.

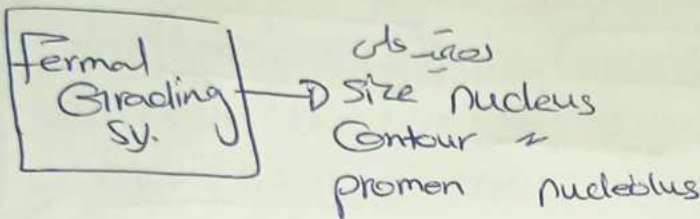
20 x 100 cm (approx) CT UL & Arteriogram UL

TNM + Grading = [] ?

STAGING AND CLASSIFICATION SYSTEMS

The Tumor Node Metastasis (TNM) classification system is recommended for clinical and scientific use, but requires continuous re-assessment.

Tumor size, venous invasion, renal capsular invasion, adrenal involvement, and LN and distant metastasis are included in the TNM classification system.

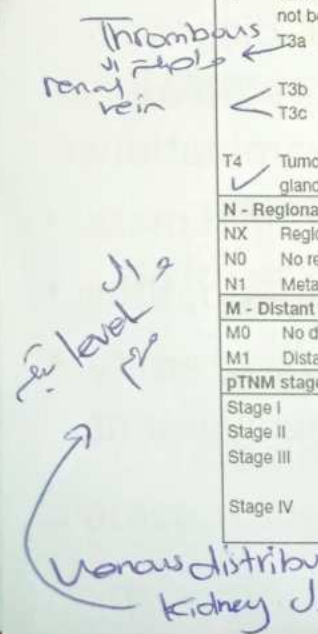
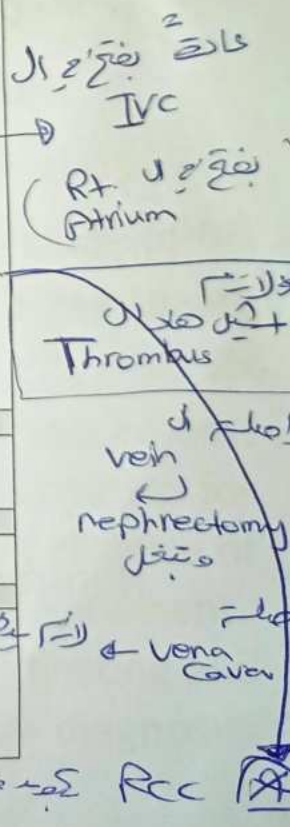


TNM Classification

T - Primary Tumour	
TX	Primary tumour cannot be assessed ✓
T0	No evidence of primary tumour ✓
T1	<u>Tumour ≤ 7 cm</u> or less in greatest dimension, limited to the kidney
T1a	Tumour ≤ 4 cm or less
T1b	Tumour > 4 cm but ≤ 7 cm
T2	Tumour > 7 cm in greatest dimension, limited to the kidney
T2a	Tumour > 7 cm but ≤ 10 cm ✓
T2b	Tumours > 10 cm, limited to the kidney ✓
T3	Tumour <u>extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota fascia</u>
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)
N - Regional Lymph Nodes	
NX	Regional lymph nodes cannot be assessed ✓
N0	No regional lymph node metastasis ✓
N1	Metastasis in regional lymph node(s) ✓
M - Distant Metastasis	
M0	No distant metastasis ✓
M1	Distant metastasis ✓
pTNM stage grouping	
Stage I	T1 N0 M0
Stage II	T2 N0 M0
Stage III	T3 N0 M0
	T1, T2, T3 N1 M0
Stage IV	T4 Any N M0
	Any T Any N M1

Vascular surgery -

(True 20)



(dislodge Thrombus see to RCC malignant cell)

آپلیکیشن کی اہم ترین بات

(True) Thrombus سے RCE

dislocated malignant cell

Venous
distribution
Kidney

level

Nephrectomy ← vein



Vena Cava

Vascular surgeon

partial

excision

bp

venous graft.

← Atrium

Cardiosurgery

para neoplastic syndromes

(10-20%)
causing

RCC
tumor

→ Abnormal

production

hormones, Enzymes, Vitamins

hypercalcemia

polythesemia

PTHrP
erythropoietin

HVT

Renin

erectile
dysfunction

female

menstrual
disturbance

GHRH

(Stawfar) Stawfar syndrome
non metastatic
hepatic dysfunction

PNs → Reversible

used

nephrectomy

← Surgery is the only way to
mortality

Surveillance is the only way to

Tissue

DIAGNOSTIC EVALUATION

Symptoms:

Many renal masses remain asymptomatic until the late

Large disease stages. More than 50% of RCCs are detected incidentally by non-invasive imaging investigating various non-specific symptoms and other abdominal diseases.

The classic triad of flank pain, visible haematuria, and palpable abdominal mass is rare (6-10%) and correlates with aggressive histology and advanced disease.

Paraneoplastic syndromes are found in approximately 30% of

Advanced RCC (Mets)
 Older age
 Spot / LLE / Jaundice / wt. loss (+)
 (lower limb edema)

Physical examination:

clinical approach of RCC

incidental finding - RCC 50% حالات ال
cholecystectomy 50% حالات ال
It kidney mass 50% حالات ال

① History ② Examination ③ Investigation

① History - Asymptomatic
[wt change, night sweat, appetite]

② Examination - general → cachexia, pallor, erythema (PCR)
① Jaundice, skin manifestation

LL edema, gynecomastia, pulmonary met
most common symptom of pulmonary met from RCC
2. non specific symptom

② Local examination:

(S lymph drainage) Palpable mass,
Para aortic - central abdominal mass (lymph node)
flank (costovertebral mass)
hypertension

③ Investigation:

Tj Labs: Urin analysis

CBC

Renal function test

S urin analysis
nephropathy - chronic kidney dz
nephrological dz
DM
nephrectomy
Kidney function
more deterioration
dialysis

biopsy

routine biopsy of renal mass, not recommended
العلاج بالbiopsy كل جديد قبل 20 سنة ما كان
أي rule و مجرد تشخيص renal mass كان في
العمل radical nephrectomy

الdiagnosis تبع الrenal center طوط عمرو
radiological diagnosis

لآخر 20 سنة ما كان أي rule biopsy

x Indication of biopsy:

- لما اكونه حاكك من الhistology انك
نزي واحد كان يحتاج وكان عنده
الabscess هاد جولد chronic و قد بعد
biopsy عنده اعد conformation حاكك انك
angio-myoma benign tumor
او حاكك انك العيان عنده tumor من other source غير ال
multiple lymph N. enlarge عنده
splenomegaly و axillary و inguinal
بعونه حاكك في lymphoma وعلاج في
nephrectomy
- انك كان indication biopsy
الmanagement صاف في حال train كان جوده
Ablative therapies او surveillance
لا اعد للعيان nephrectomy من العيان لو كان comorbid
وعنه very small lesion و الwave ال
rest benefit nephrectomy

Polycythemia anemia CBC من قبل الجراح
base line kidney function -
nephrectomy

diagnosis confirmation
renal mass inadequate characterization
with IV contrast CTU
renal function impaired
contrast

labs other investigation
Ca, liver function

② Imaging

CT with contrast

US CT

renal mass adequate characterization
accurate

location of mass
size management

malignant benign
contrast enhancement
mass uptake

vascular mass
kidney
consider malignancy biopsy

suprarenal involvement

lymph node

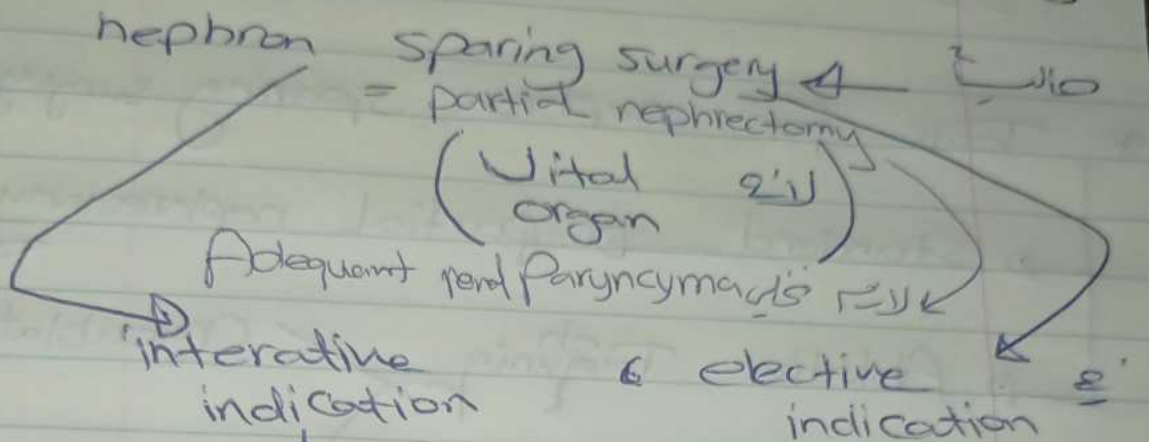
present & function of contralateral kidney

nephrectomy

Management :-

Gold Standard → Radical nephrectomy

organ
+
surviving T.



- Solitary kidney

- Bilateral tumor synd. UI

Tumor
peripheral T1

< 4cm

- poor overall kidney function

- Normal kidney

signs of renal disease
nephropathy

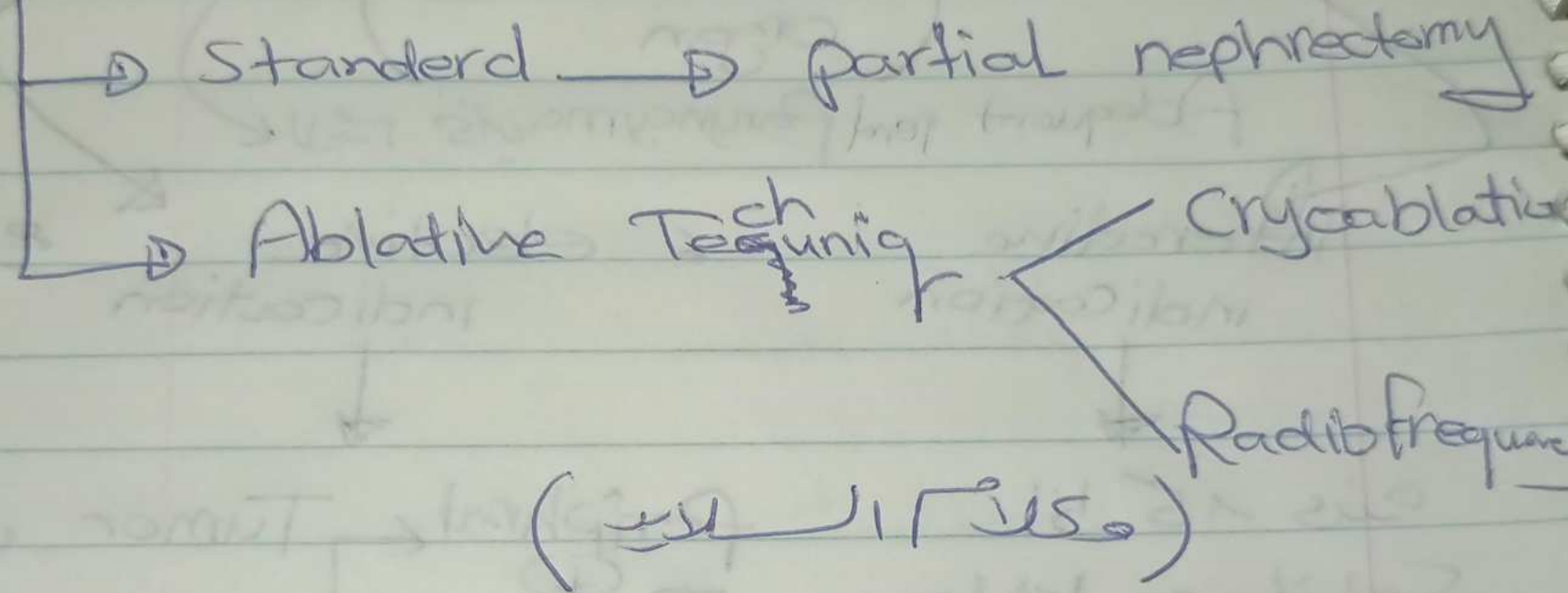
DM

نحفظ الكلى
nephron
sparing

إلى الكلية
إلى الكلية

عملية
Radical
operation

Tools for nephron sparing surgery



Under US / CT guid
Laparoscopic
(-40) freezing

Ablative therapies: .1

Cryoablation: ➤

Cryoablation is performed using either a percutaneous or a laparoscopic-assisted approach.

In comparative studies, there was no significant difference in the overall complication rates between laparoscopic- and percutaneous cryoablation.

Radiofrequency ablation: ➤

Radiofrequency ablation is performed laparoscopically or percutaneously. Four studies compared patients with T1a tumors treated by laparoscopic or percutaneous RFA.

heating (105°) mass Guid

Tissue necrosis

enhancement. CT + In Contrast

Other ablative techniques: ➤

Some studies have shown the feasibility of other ablative techniques, such as microwave ablation, laser ablation, high-intensity focused US ablation and irreversible electroporation. However, these techniques are considered experimental.

other indication for biopsy Advanced D. or malignant D.

Advanced/metastatic RCC

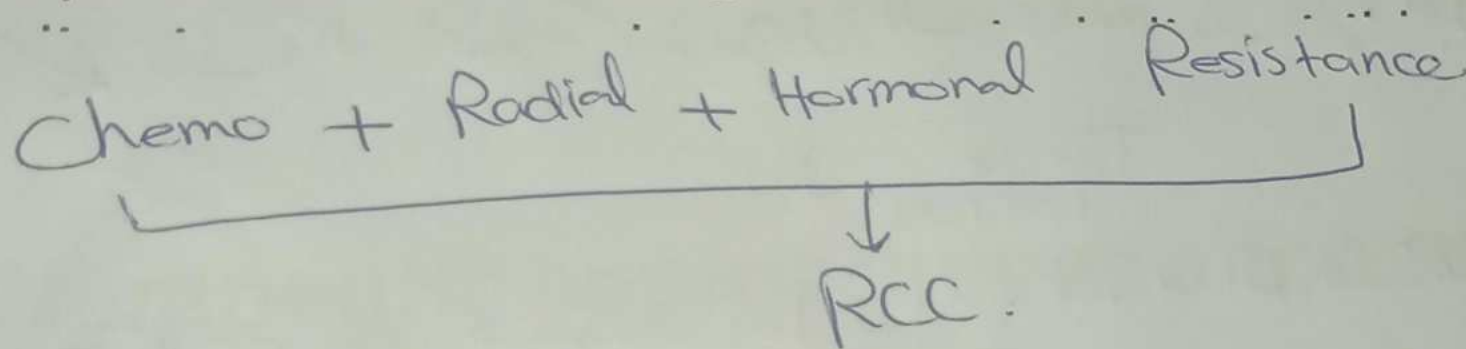
Local therapy of advanced/metastatic RCC

* **Cytoreductive nephrectomy:**

Tumor resection is potentially curative only if all tumor deposits are excised. This includes patients with the primary tumor in place and single- or oligometastatic respectable disease. For most patients with metastatic disease, cytoreductive nephrectomy (CN) is palliative and systemic treatments are necessary.

~~THE~~ * **Embolization of the primary tumor:**

In patients unfit for surgery or ^{Angio}with non-resectable disease,



Solitary 5131 Excision ^{Angio} ← Metastasis (*)

Advanced/metastatic RCC

Monoclonal antibody against circulating VEGF

Bevacizumab monotherapy and bevacizumab plus IFN- α :

Bevacizumab is a humanised monoclonal antibody.

The double-blind AVOREN study compared bevacizumab plus IFN- α with IFN- α monotherapy in mRCC. Overall response was higher in the bevacizumab plus IFN- α group.

→ Affect

clear cell RCC.

→ disadvantage → delay wound healing

⊕ Irreversible change in voice.

mTOR inhibitors

Temsirolimus:

Temsirolimus is a specific inhibitor of mTOR. Its use has been superseded as front-line treatment option.

Everolimus:

Everolimus is an oral mTOR inhibitor, which is established in the treatment of VEGF-refractory disease. The RECORD-1 study compared everolimus plus best supportive care (BSC) vs. placebo plus BSC in patients with previously failed anti-VEGFR treatment (or previously intolerant of VEGF-targeted therapy).

Clear cell
immune therapy
Temsirolimus
cheek bone
PCD
programme
cell death

BEST