Greater Manchester and Cheshire NHS

Cancer Network

RENAL CANCER GUIDELINES

Agreed by Urology CSG: July 2010
Review Date: July 2012

Renal Cancer Guidelines

1. Introduction

1.1 Kidney cancer accounts for 3% of all new cases of cancer diagnosed in men and almost 2% of all major cancers in women in the UK.

1.2 There is an approximate male: female ratio of 3:2.

1.3 Incidence of kidney cancer is rising in the UK, particularly in the elderly population. This increase is seen both in males and females.

Table 1.1: Number of new cases and rates of kidney cancer, UK, 2005

	England		Wales		Scotland		N.Ireland		UK	
Cases										
Males	3,822		284		413		103		4,622	
Females	2,244		160		280		74		2,758	
Persons	6,066		444		693		177		7,380	
Crude rate per 100,000 population										
Males	15.4		19.7		16.8		12.2		15.7	
Females	8.7		10.6		10.6		8.4		9.0	
Persons	12.0		15.0		13.6		10.3		12.3	
Age-standardised rate (European) per 100,000 population										
Males	13.2		15.6		14.2		11.8		13.4	
CI 95%	*12.8*	*13.6*	*13.8*	*17.4*	*12.8*	*15.5*	*9.6*	*14.1*	*13.0*	*13.8*
Females	6.5		7.3		7.2		6.9		6.6	
CI 95%	*6.2*	*6.8*	*6.2*	*8.4*	*6.3*	*8.0*	*5.3*	*8.4*	*6.4*	*6.9*
Persons	9.6		11.1		10.4		9.0		9.7	
CI 95%	*9.3*	*9.8*	*10.1*	*12.2*	*9.6*	*11.1*	*7.7*	*10.3*	*9.5*	*9.9*

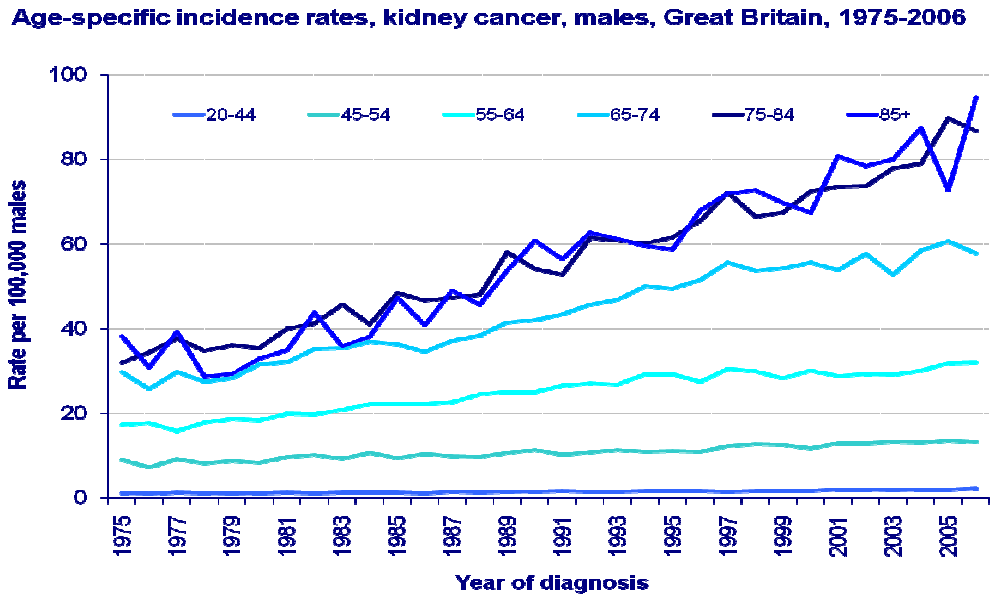
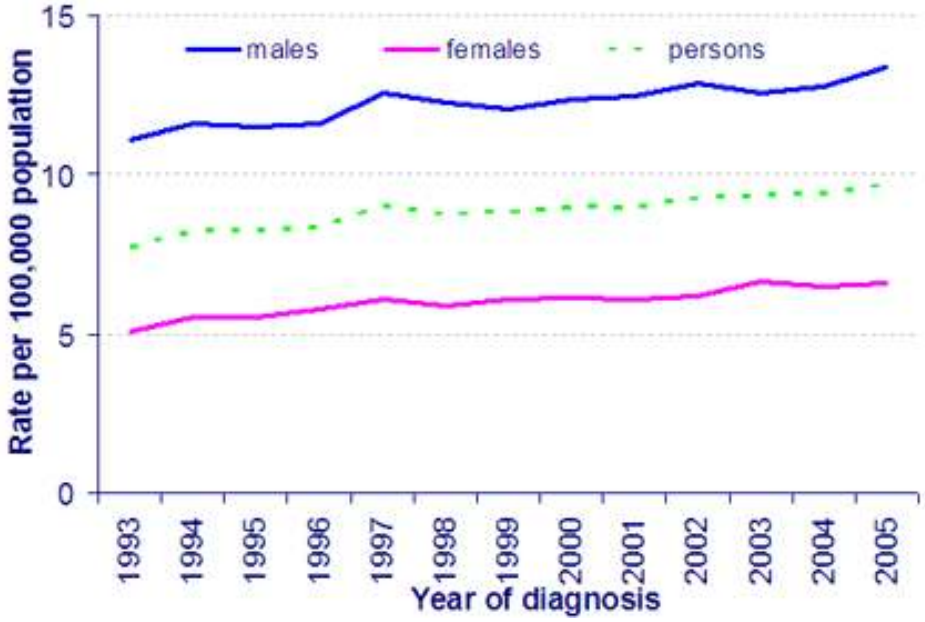


Figure 1.9: Age standardised (European) incidence rates, kidney cancer, by sex, UK, 1993-2005

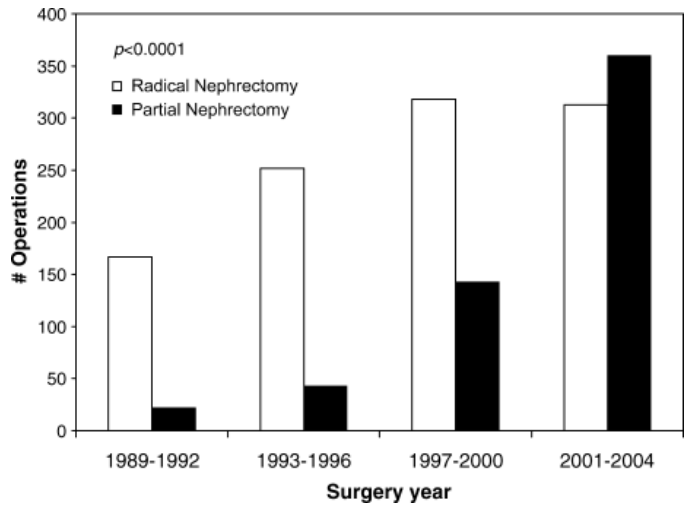


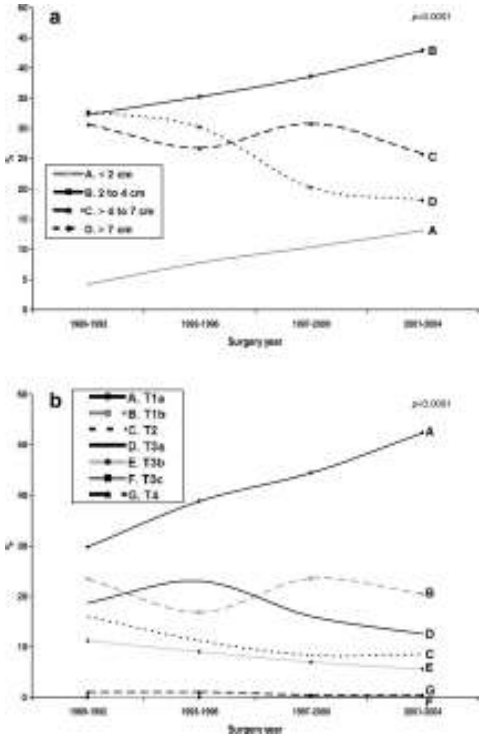
1.4 Kidney cancer is the ninth commonest cancer death in men, and the thirteenth commonest in women. It accounts for approximately 2% of all cancer deaths in the UK.

1.5 Kidney cancer mortality rates have risen in the UK since the 1970s. Death rates increase with increasing age and majority occur in the over 60s.

1.6 Renal cancer is associated with obesity and cigarette smoking. All patients encountered should therefore be encouraged and given help in smoking cessation and weight loss.

1.7 There has been a global increase in the detection and treatment of incidentally diagnosed renal masses in developed countries. This is exemplified by the published data from the Memorial Sloan Kettering Cancer Centre shown below (Russo et al Cancer 2008).





2. Clinical Assessment

2.1 Many cases are now identified incidentally and are asymptomatic. All should be investigated according to protocol as described below. Any associated Haematuria requires full investigation according to local protocol.

2.2 History should include previous operations, medical conditions such as diabetes, hypertension which may affect renal function, co-morbidities which may affect surgical management, and symptoms which may reflect metastatic disease or effects arising as a consequence of a paraneoplastic syndrome; e.g. bone pain, haemoptysis, PUO, cachexia.

2.3 Thorough physical examination should be undertaken. The patient's blood pressure should be recorded. A palpable mass or signs of vascular invasion may be sought including the presence of a non-reducing varicocoele, DVT or other signs of chronic IVC obstruction.

2.4 All patients should have a FBC and biochemical profile performed as a minimum.

2.5 Patients <50 years with multiple renal tumours or a family history of RCC should be considered for genetic screening for Von Hippel Lindau or other familial renal diseases.

3. Radiological Assessment

3.1 Many cases will be identified incidentally on ultrasound examination or cross sectional imaging for another condition. All solid lesions and complex cystic lesions require further imaging.

3.2 The main modality for assessment of renal masses is pre- and post-contrast enhanced multi-slice CT scanning. The scan should incorporate the abdomen and pelvis. Assessment should include statements regarding the characteristics of the primary tumour (size, character, location, renal and local anatomy), loco regional lymph nodes (number, size, location), adrenal and peri-renal anatomy (liver, pancreas/biliary tree, duodenum, colon and spleen). The renal vasculature anatomy should be addressed specifically, particularly with regard to the presence or absence of renal vein/ IVC invasion.

3.3 A thoracic CT scan is also recommended as part of the CT scan protocol to assess the presence or absence of pulmonary metastases.

3.4 Bone scanning is not routinely recommended unless there is clinical or biochemical suspicion of bony metastatic disease (bone pain, abnormal serum alkaline phosphatase, hypercalcaemia). Cross sectional imaging with MR or CT is also useful in detecting and assessing bone metastases in many cases and these imaging modalities should be considered in the assessment of bony disease.

3.5 Magnetic resonance imaging may be helpful in assessment of vena caval thrombus extent or for clarifying the anatomy of specific lesions within the kidney.

3.6 Radio-isotopic renal function assessment, including split renal function, may be considered in patients with impaired function undergoing nephrectom or nephron-sparing surgery.

4. Management

4.1 All cases should be discussed at a Unit MDT for management planning, with specific cases referred for discussion at a Specialist MDT. Simple renal tumours requiring uncomplicated nephrectomy may be managed at local units. Complex renal cancer must be managed at a specialist centre. As defined by the IOG Guidance the following types of case are considered as complex and must be referred for discussion and treatment planning by the Specialist MDT:

- Patients whose tumours are suitable for nephron sparing surgery
- Patients requiring nephro-ureterectomy
- Tumours in single systems
- Patients with Multiple or bilateral Renal Tumours
- Tumours with renal vein and/or IVC involvement
- Patients undergoing debulking nephrectomy
- Patients with Von Hippel Landau Disease

4.2. Management of Localised Disease

4.2.1 The preferred treatment for localised renal cancer is surgical. Where possible renal tissue and therefore global renal function should be

preserved by using a nephron sparing approach. A body of evidence has now shown that the risks of co-morbid cardiovascular events are increased significantly in patients undergoing nephrectomy by comparison with those treated with a nephron sparing approach and that renal ablation by total nephrectomy for most renal masses of 4cms or less is inappropriately radical treatment.

4.2.2 Nephron-sparing surgery should be considered in the following indications:

Absolute:

- The presence of an anatomical or functional solitary kidney.
- Chronic renal insufficiency whereby nephrectomy would result in need for dialysis.
- Bilateral and/or multiple renal cancers
- Patients with von Hippel Landau disease or other genetic conditions with a predisposition resulting in likelihood of developing further tumours in the future. These rare conditions should be focussed through the Salford SMDT.

Relative:

- The presence of a well circumscribed tumour or tumours with a functioning contra-lateral kidney

4.2.3 Laparoscopic nephrectomy should be considered when a nephron sparing approach is not possible and there is no contra-indication to laparoscopy.

4.2.4 Open radical nephrectomy is the treatment of choice for large renal tumours, especially in the presence of renal vein invasion. Adrenalectomy is not necessary if pre-operative imaging confirms a normal ipsilateral adrenal gland, except in upper pole tumours, where there is a greater risk of invasion, or in tumours>7cm where there is an augmented risk of metastatic spread. Tumours with a higher degree of complexity (e.g. bowel, liver, pancreatic, splenic involvement) should be referred to a specialist centre for evaluation.

4.2.5 Patients with renal vein and / or IVC involvement should be referred to a centre with experience in the management of these complex cases. Cases with supra-hepatic involvement should be referred to the Salford / Wythenshawe team for joint operation operating with the Wythenshawe cardiothoracic surgical team where tumours require cardiopulmonary bypass.

4.2.6 Patients with pre-existing CKD and a potential requirement for post surgical dialysis should be referred to centres with co-existing nephrology services, with facilities for optimisation of renal function pre-operatively and for dialysis post-operatively when required.

4.2.7 Patients with severe co-morbidities precluding surgery should be monitored and palliative treatment offered as appropriate; e.g. embolisation, palliative radiotherapy, supportive care.

4.2.8 Minimally invasive treatment including radiofrequency ablation, and laparoscopic or percutaneous cryotherapy are still considered as experimental therapies and should only be used in association with advice produced by NICE that standardised protocols should be adopted and the outcome results and complications recorded routinely as part of a written investigational protocol.

4.2.9 Specialist urology nurse involvement should be available at an early stage and their involvement recorded in the documentary record. MacMillan nurse support and/or palliative care team involvement may be indicated in specific patient journeys.

4.3 Metastatic disease

4.3.1 Patients with good performance status and low metastatic disease load may be considered for debulking nephrectomy as an adjunct to subsequent systemic therapy. Discussion at the Supranetwork MDT should be considered before advocating such surgery to assess whether surgery is appropriate and/or feasible and to determine the most likely non-surgical intervention. Surgery of this type may be challenging and should only be performed in centres familiar with this type of therapeutic approach.

4.3.2 Solitary metastases may be considered for local resection (metastasectomy). Discussion at the Christie SnMDT is required before definitive decisions relating to this are made.

4.3.3 Patients not suitable for surgical intervention should be considered for referral for systemic treatment, either with immunotherapy or other targeted therapies using sunitinib as the drug of first choice in the absence of a clinical trial.

4.3.4 Palliative care team referral should be offered at an early stage for patient support and symptom control as appropriate.

5. Surveillance following Surgery for RCC

5.1 Pathological Staging – Histopathology reports for RCC should include the following as a minimum:

- Histological type
- Furhmann Grade
- Pathological Stage using the most recent TNM system
- Tumour size
- Presence or absence of necrosis
- Presence or absence of sarcomatoid changes

- In clear cell tumours, % of clear cell: granular cell ratio
- Information relating to renal vein / IVC invasion when this is present
- Specific statements about tumour margins in nephron sparing cases

5.2 Patients should be stratified into risk groups for development of metastatic disease and a standardised follow-up protocol implemented such as the Mayo risk score should be considered for adoption (see below). Patients with high risk features should be considered for counselling with a view to entry in to the NCRI SORCE trial.

5.3 Patients developing metastases on surveillance should be discussed at an SMDT for consideration regarding suitability for further non-surgical systemic therapy or surgical treatment, including metastasectomy. Palliative care team/ MacMillan referral may be appropriate.

6. Pathology Reporting

6.1 All cases shall be reported in accordance with the Royal College of Pathologists standards and datasets. This document can be found at www.rcpath.org.uk and in the network guideline document "Pathology Guidelines for Urological Cancers".

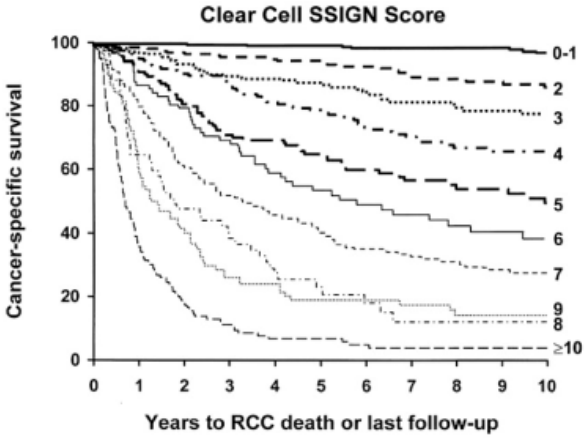
Prognosis tables and follow up plans for Renal Cancer

SRH Foundation Trust
Agreed 20.04.2007
D C Shackley, M W Lau, N W Clarke

The **prognosis** for clear cell RCC following nephrectomy can be calculated on the SSIGN algorithm[1] below which has been externally validated[2]. The prognosis for non-clear cell RCC post-kidney removal can be evaluated with the Kattan[3] system though the latter system only gives a progression-free survival rather than cancer-specific survival.

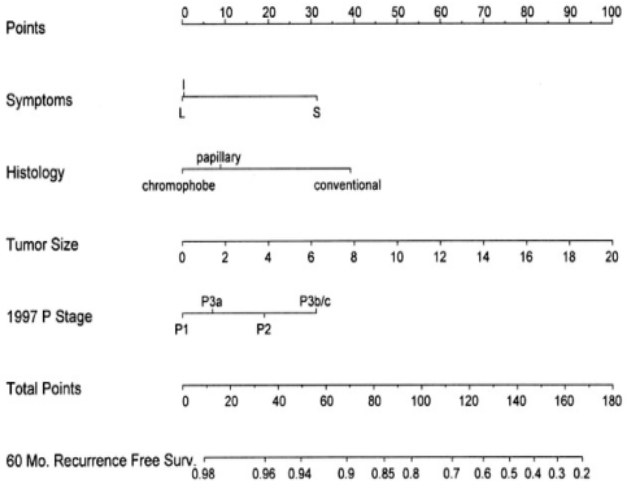
SSIGN: the algorithm (table) and subsequent cancer-specific survival based on this algorithm (Kaplan-Meier plot).

Feature	Score
T stage:	
pT1	0
pT2	1
pT3a	2
pT3b	2
pT3c	2
pT4	0
N stage:	
pNx	0
pN0	0
pN1	2
pN2	2
M stage:	
pM0	0
pM1	4
Tumor size (cm.):	
Less than 5	0
5 or Greater	2
Nuclear grade:	
1	0
2	0
3	1
4	3
Necrosis:	
Absent	0
Present	2



Five-year cancer-specific survival rates[2] in patients with a score of:
0 to 2 (100%),
3 to 4 (90%)
5 to 6 (64%)
7 to 9 (47%)
10 (0%) in clear cell RCC

The Kattan nomogram



Instructions for Physician: Locate the patient's symptoms (I=incidental, L=local, S=systemic) on the Symptoms axis. Draw a line straight upwards to the **Points** axis to determine how many points towards recurrence the patient receives for his symptoms. Repeat this process for the other axes, each time drawing straight upward to the **Points** axis. Sum the points achieved for each predictor and locate this sum on the **Total Points** axis. Draw a line straight down to find the patient's probability of remaining recurrence free for 5 years assuming he or she does not die of another cause first.

Instruction to Patient: "Mr. X, if we had 100 men or women exactly like you, we would expect between <predicted percentage from nomogram – 10%> and <predicted percentage + 10%> to remain free of their disease at 5 years following surgery, though recurrence after 5 years is still possible."

[1] An outcome prediction model for patients with *clear cell* renal cell carcinoma treated with radical nephrectomy based on tumor stage, size, grade and necrosis: The SSIGN score: Frank I, Blute ML, Cheville JC, Lohse CM, Weaver AL, Zincke H JOURNAL OF UROLOGY 168 (6): 2395-2400 DEC 2002

[2] External validation of the Mayo Clinic Stage, Size, Grade and Necrosis (SSIGN) score to predict cancer specific survival using a European series of conventional renal cell carcinoma. Ficarra V, Martignoni G, Lohse C, Novara G, Pea M, Cavalleri S, Artibani W. JOURNAL OF UROLOGY 175 (4): 1235-9: 2006

[3] A postoperative prognostic nomogram for renal cell carcinoma: Kattan MW, Reuter V, Motzer RJ, Katz J, Russo P. JOURNAL OF UROLOGY 166 (1): 63-67 JUL 2001

The **risk of metastases** can be calculated using the MAYO system [Leibovich BC, Blute ML, Zincke et al: Cancer 2003;97:1663-71] below:

Mayo scoring system:

T stage	**Score**
pT1a	0
pT1b	2
pT2	3
pT3/4	4
Tumour size	
<10cm	0
>10cm	1
Nodal status	
pNx or N0	0
pN1/2	2
Grade (Fuhrmann)	
1-2	0
3	1
4	3
Necrosis	
No	0
Yes	1

Total score is added:

Low risk: 0-2

Intermediate: 3-5

High risk >6

Accumulated risk metastases (%):

Risk gp	yr1	yr 3	yr5	yr10
Low	*<1*	*2*	*3*	*7.5%*
Intermediate	*10*	*20*	*26*	*36%*
High	*42*	*63*	*69*	*76%*

Guidelines: (From the EAU 2006 guidelines)

(1) All patients should be discussed at MDT with pathology post-operatively with relevant algorithms calculated at that visit.
(2) All patients reviewed in OPC at 4-6 weeks to assess complications, discuss histology and clarify follow-up protocol with patient.
(3) All patients at this initial 4-6 week visit should have serum Creatinine checked as baseline together with BP. Also, IF the alkaline phosphatase was raised preoperatively (or any other LFT) then this should be repeated at this visit).
(4) Patients should be seen 6/12ly for the first 5 years and then annually to 10 years.

FOR CLEAR CELL:
(1) The SSIGN score will be calculated to find out the 1 through 10-year respective cancer-specific survival rates and perhaps quote the 5-yr rates in the MDT correspondence.
(2) The Mayo metastatic scoring system should be used to attribute the low intermediate or high risk status to patients in order to clarify a follow-up plan:

- **Low**: Every clinic visit to have Creatinine, BP and clinical assessment. CXR and US should be performed* annually.
- **Intermediate:** Every clinic visit to have Creatinine, BP and clinical assessment. At 5/12, 18/12, 3 years to have CT chest/ abdo then annual US and CXR thereafter.
- **High:** Every clinic visit to have Creatinine, BP and clinical assessment. To have CT thorax and abdo every 6/12 to 3 years then annual US and CXR thereafter.

FOR OTHER RENAL TUMOURS:

- Use the KATTAN nomogram and apportion approximate risks for developing metastases by 5 years.
- Classify in a similar way to MAYO above with the same percentages i.e. If risk of metastases are low single figures (e.g. <5% at yr 5) then they should be LOW risk; If risk is 5-25% then INTERMEDIATE and >25% HIGH.
- Once classified then the follow up will be as clear cell above.

DS 20/04/2007