Surgical Management of Renal Cancer

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The Royal Marsden
NHS Foundation Trust
Surgery for Kidney Cancer

Roles of Surgery

1. Curative intervention – localised disease
2. Symptomatic control – advanced disease
3. Augmentation of efficacy of systemic therapy – advanced disease
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Radical Nephrectomy is only potentially curative treatment for renal cell carcinoma!!!

Robson

*J Urol*

1963;89:37-42

? Has much changed in 50 years
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Spectrum of Disease

1. Small renal masses
2. ‘Clinically significant’ tumours with no evidence of metastases
3. Metastatic RCC
   1. Asymptomatic tumour
   2. Symptomatic tumour
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1. Small renal masses

Detected as incidental findings
Natural history often slow progression + low risk of metastatic disease if < 3-4cm
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2. ‘Clinically significant’ tumours

In absence of spread Robsons conclusion remains true
Surgical excision – usually nephrectomy remains treatment of choice
   Laparoscopic approach – case selection
Open surgery
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3. Metastatic RCC
   Symptomatic tumour

   Surgery – often most effective palliation

   Asymptomatic tumour

   ? Rationale for surgery in the context of extra-renal disease
   ? Role in conjunction with systemic therapies
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1960’s - Dialysis
1970’s - Partial nephrectomy
1980’s – IL2/interferon
1990’s – Laparoscopic nephrectomy
2000’s -
  - Cytoreductive nephrectomy
  - Elective partial nephrectomy
  - Ablative therapies
  - Targeted therapies
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Level 1 Evidence – limited to 3 trials

2 trials showing nephrectomy + IFN improved survival to IFN alone

* generally interpreted as nephrectomy improves survival
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1 trial - nephrectomy vs partial for T1 tumours with normal contralateral kidney.

Higher complications with PN
No increased risk of cardiovascular or renal failure related outcomes with RN

* Generally ignored
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Epidemiological data

1. Increased incidence of (diagnosed) RCC
2. Profound stage shift to T1 disease
3. No improvement in overall mortality – no change in numbers presenting with metastatic disease
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Observational data – tumours <3-4cm

1. Low incidence of metastastic disease
2. Slow growth in many patients(<1cm/year)
3. Minimal risk of metastatic disease with surveillance and intervention with demonstrated growth
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T1 disease – increased options

1. Partial nephrectomy
2. Ablative therapies
3. Surveillance in selected patients
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Partial nephrectomy
Open – morbidity
Laparoscopic – feasible but difficult
Robotic – available at selected institutions*

* Urological focus – driven by urologists, institutions, industry
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Ablative therapies – Percutaneous (??Lap)
Cryotherapy/Radiofrequency ablation
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Ablative therapies –
- cryotherapy/radiofrequency ablation

10% local failure (i.e., persistent tumour)
Nephrectomy usual outcome if subsequent surgery
Size/anatomical limitations

* Good option for selected patients with small lesion/failed surveillance
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T2 Tumours

Nephron sparing approaches potentially compromise surgical outcomes

Laparoscopic/Open Nephrectomy OR
Open Partial (imperative indication)
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T3 Tumours

1. Intravascular tumour

2. Nodal disease
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Tumour Thrombus

Surgical excision often feasible

May require cardiopulmonary bypass

Prognosis related to N/M status
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Lymphadenectomy - EORTC - 30881

772 patients with T1-3 N₀M₀
• RN vs RN + LND
• No difference in CSS
BUT
• High prevalence of low risk disease
• Only 3% have LN+
• Few patients (17%) – progressed/died

Underpowered – difficult to draw conclusions

Blom et al
Eur Urol 2009
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Lymphadenectomy – N0M0

EORTC/SEER – no benefit with clinical non-involved nodes
Institutions – benefit in ‘high’ risk cases

Mayo Clinic
• High T stage – T3, T4, High Fuhrman grade 3, 4
• Large size (>10cm), Histological tumour necrosis
* Advocate intra-operative frozen section
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Lymphadenectomy – N+M0

Institutional series reports of patients undergoing extensive LND with
• Improved CSS
• Long term survival

But
• Non-randomised
• Median improvement @ 5 months
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MD Anderson - 40 patients
• Extended dissection
• Only included COMPLETE resections
• Median CSS 20.3 months

Canfield et al
J Urol 2006
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Lymph Node Disease - Autopsy series
(death from other causes)
• 554 patients with RCC
• 80(14%) had LN+ disease

BUT only 5 had exclusively para-aortic or paracaval

Johnsen & Hellsten
J Urol 1997
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Left
• Crus to aortic bifurcation

Right
• Paracaval + interaortocaval

Parker, AE
American J Anat 1935
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No uniformly accepted guidelines on extent or anatomic boundaries when performed as an adjunct to radical nephrectomy

Staging accuracy correlates with extent of dissection/number of nodes

Crispen et al
Eur Urol 2011
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Lymphadenectomy – N+M0

5 year CSS
- 18% - extracapsular nodal disease
- 35% - without extracapsular nodal disease

Dimashkeh et al
J Urol 2006
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Lymphadenectomy –

Appears of no benefit in T1-2 disease if cN0

Poor evidence base outside these parameters

Possibly consider in high risk (>10cm, necrosis) if cN0/N1
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Cytoreductive Nephrectomy (CRN)

<table>
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<tr>
<th></th>
<th>N</th>
<th>Survival (med) N</th>
<th>Survival (med) N + IFN</th>
<th>Survival (med) IFN alone</th>
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2 trials showing nephrectomy + IFN improved survival to IFN alone

* Generally (mis)interpreted as nephrectomy improves survival
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*P values for the comparison of median survival between groups were derived with the log-rank test.
†Performance was scored as 0 or 1, with 1 indicating decreased activity.
**Table 2. Survival in Subgroups Defined According to Stratification Factors.**

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NNT - 8 patients undergo surgery for ONE additional patient to survive at 12 months.
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Cytoreductive Nephrectomy

UCLA – 1989-2006
418 patients
ECOG PS
0 – n=117, 26.7 months
1 – n=274, 13.8 months
2/3 – 27, 6.8 months

Shuch et al
Cancer 2008
Surgery for Kidney Cancer

Cytoreductive Nephrectomy

Outcome better if ECOG 2/3 status related to painful bone metastases rather than visceral disease

17.7 vs 2.1 months

Shuch et al, Cancer 2008
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Metastatic disease

Patient scenarios

1. Symptomatic primary ✓

2. Asymptomatic primary ?
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Asymptomatic Primary

ECOG PS > 1 - not of benefit/potentially harmful

ECOG 0 – no evidence at present time

CARMENA (Sutent vs CRN + Sutent)

Other trials
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Asymptomatic Primary

Low Volume Disease
No definite evidence
Possibly an initial intervention particularly if there is consideration for deferring systemic therapy

High Volume Disease
May not be advantage
Could delay systemic therapy
Consider if response to systemic treatment and good PS
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Lymphadenectomy with CRN?
Suggestion of improved survival
Limited to institutional series
Selection bias ++

UCLA – CRN + IL2
129 patients – N+M+
5 month survival advantage with LND

NCI – CRN + IL2
82 pN –ve; 72 pN +ve
Median survival 14.7 vs 8.5 months

Survival – no difference between pN+ with LND and complete resection and pN0
Vasselli et al
J Urol 2001
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57% of patients treated with cytoreductive nephrectomy + LND were pN$_0$

Lack of lymphadenopathy predicts survival of patients with metastatic disease


UCLA

Survival of N+M0 equivalent to N0M+

N+M+ survival $<<$ both N+M0 and N0M+


3 years cancer specific survival with cytoreductive nephrectomy + LND

pN$_0$ - 34.7%
pN$+$ - 14.4%

Lughezzani et al, *Cancer* 2009
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Summary
Surgery remains the most reliable curative intervention for RCC

Most RCC requiring intervention are small localised tumours

Nephron sparing approaches including surveillance, ablative non-surgical interventions and minimally invasive surgical techniques increasingly utilised.
Surgical Issues in RCC

Summary
Role of CRN including timing and indications yet to be determined for metastatic disease

Lymphadenectomy role also requires clarification

Lymph node status may be a significant confounder for which stratification is required in future surgical and systemic therapy trials.
Surgical Issues in RCC
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