Lymphadenectomy Is Important In Metastatic Renal Cell Carcinoma: PRO

Christopher G. Wood, M. D., FACS
Professor and Deputy Chairman
Douglas E. Johnson, M. D. Professorship in Urology
Department of Urology
The University of Texas MD Anderson Cancer Center
Two Clinical Scenarios

- Cytoreductive nephrectomy in the setting of clinically negative lymph nodes
  - Is there any indication to do a lymph node dissection?

- Cytoreductive nephrectomy in the setting of clinically positive lymph nodes
  - Does removal of the nodal disease, in addition to the primary tumor, improve outcome?
LND in Metastatic RCC

• Why?
  – May be prognostic in the setting of M1 disease
  – Might be therapeutic
  – May guide subsequent therapy decisions
  – No added morbidity

• Why Not?
  – May add morbidity and delay therapy
  – How can it be therapeutic in the setting of distant mets?
  – Information gained is not worth the effort; Doesn’t guide therapy decisions
LND in Metastatic RCC

• Is definitely prognostic!

• May be therapeutic, especially in the setting of clinically or pathologically positive lymph nodes

• Information gained from LND may guide subsequent therapy decisions
  • Metastasectomy versus systemic therapy
  • What type of systemic therapy?

• Little to no added morbidity associated with a limited template dissection
Lymph Node Metastases In The Setting Of Distant Metastases Is Associated With A Very Poor Outcome!

Knowledge of Nodal Status is Prognostic.
Presence of Nodal Metastases In Metastatic Renal Cell Carcinoma Predicts Survival

N- (82 pts): 14.7 mos
N+ (72 pts): 8.5 mos

Overall Survival for RCC Patients With and Without Nodal Metastases

Pantuck et al., J Urol, 2003
Identifying Patients who will Not Benefit from Cytoreductive Nephrectomy: MDACC

- 566 pts undergoing CN between 1991 and 2007
- 110 pts undergoing medical therapy only
- Compared survival between groups and identified when survival diverged between surgical and non-surgical groups
- Identified pre-operative variables that differed between surgical groups based on follow-up
- Pre-operative “Risk Factors” based on significance in multivariate analysis

Culp et al., Cancer, 2010
Surgery vs. No Surgery

Overall Survival

Overall Survival Based on Follow-up of 8.5 months

Culp et al., Cancer, 2010
Risk Factors Significant in MVA

- Serum albumin < lower limit of normal
- Serum LDH > upper limit of normal
- Liver metastasis
- Symptoms at presentation due to metastasis
- Retroperitoneal lymph node involvement
- Supra-diaphragmatic lymph node involvement
- Clinical T stage 3 or 4

Culp et al., Cancer, 2010
The Presence of Nodal Metastases Predicts Outcome in mRCC

Cytoreductive Nephrectomy In The Era of Targeted Therapy (SEER 2005 – 2009)

Predictive Clinical Factors
1. Size > 7 cm
2. cT3 or cT4 Stage
3. High grade (3 or 4)
4. Positive lymph nodes
5. Sarcomatoid Histology

Culp and Wood, Submitted
Can a lymph node dissection alter outcomes in the setting of metastatic disease?
Volume of Retroperitoneal Adenopathy and Resectability Influence Survival In Metastatic Renal Cell Carcinoma

Survival (mos) (p=0.045)

- < 50 cm³: 10.5
- > 50 cm³: 5.3

Survival (mos)

1. Complete resection (n=13) – 8.6
2. Incomplete resection (n=29) – 8.5
3. Unresectable (n=5) – 3.3
4. Unknown volume (n=25) – 9.3

N+(resected) vs. N- (p=0.07)

Importance of LN Dissection in Renal Carcinoma

Clinical Evidence Of Nodal Metastases
*No difference in RFS, M status not specified

Pantuck A et al, J Urol, 2003
Resection Of Retroperitoneal Nodal Metastases In Patients With Metastatic Conventional Renal Cell Carcinoma: The MDACC Experience

- 1990 to 2007
- $322 - T_{\text{any}}N_0M_1$
- $55 - T_{\text{any}}N_{1-2}M_1$
- Clear cell histology
- Retroperitoneal adenopathy only
<table>
<thead>
<tr>
<th></th>
<th>Hazard Ratio (95% CI)</th>
<th>P</th>
<th>Median Survival (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$N_0M_1$</td>
<td>Referent</td>
<td>--</td>
<td>28.4</td>
</tr>
<tr>
<td>$N_{1-2}M_1 + \text{LND}$</td>
<td>1.53 (1.04, 2.25)</td>
<td>0.03</td>
<td>18.3</td>
</tr>
<tr>
<td>$N_{1-2}M_1 \text{ No LND}$</td>
<td>3.10 (1.95, 4.91)</td>
<td>&lt;0.001</td>
<td>9.8</td>
</tr>
</tbody>
</table>
What about performing a lymph node dissection in the setting of clinically negative lymph nodes?
Knowledge of Nodal Status May Guide Therapy Decisions

• Dr. Michael Blute; KCA Meeting, Chicago, 2012: “I perform a node dissection during CN to guide my use of metastasectomy. If the nodes are positive, I am less likely to offer metastasectomy because of their overall poor prognosis.”

• Knowledge of nodal status may guide choice of systemic therapy (immunotherapy versus targeted therapy)

• Finding pathologically positive lymph nodes will impact prognosis and perhaps response to therapy
  • Patient deserves to know what they are up against
Does performing a lymph node dissection add morbidity to a cytoreductive nephrectomy?
• When performing LND,
  • the paracaval and inter- aortocaval lymph nodes be removed in patients with **right-sided tumors**
  • the para-aortic and interaortocaval lymph nodes be removed in patients with **left-sided tumors**
  • from the crus of the diaphragm to the common iliac artery.
### Table 3 – Complications of surgery in eligible patients

<table>
<thead>
<tr>
<th></th>
<th>Without lymph-node dissection (n = 370)</th>
<th>With complete lymph node dissection (n = 362)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Bleeding &gt;1 l</td>
<td>24</td>
<td>6.5</td>
</tr>
<tr>
<td>Pleural damage</td>
<td>19</td>
<td>5.1</td>
</tr>
<tr>
<td>Infection</td>
<td>21</td>
<td>5.7</td>
</tr>
<tr>
<td>Bowel damage</td>
<td>5</td>
<td>1.4</td>
</tr>
<tr>
<td>Embolism</td>
<td>4</td>
<td>1.1</td>
</tr>
<tr>
<td>Lymph fluid drainage</td>
<td>9</td>
<td>2.4</td>
</tr>
<tr>
<td>Total</td>
<td>82</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions

• Performing a lymph node dissection at the time of cytoreductive surgery can be prognostic, therapeutic, can be used as a guide to choose subsequent therapy, and does not add significant morbidity to the operation.

• In the absence of level 1 data, “Can’t hurt, might help, why not?”