Lymphadenectomy Is Important In Metastatic Renal Cell Carcinoma: PRO

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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

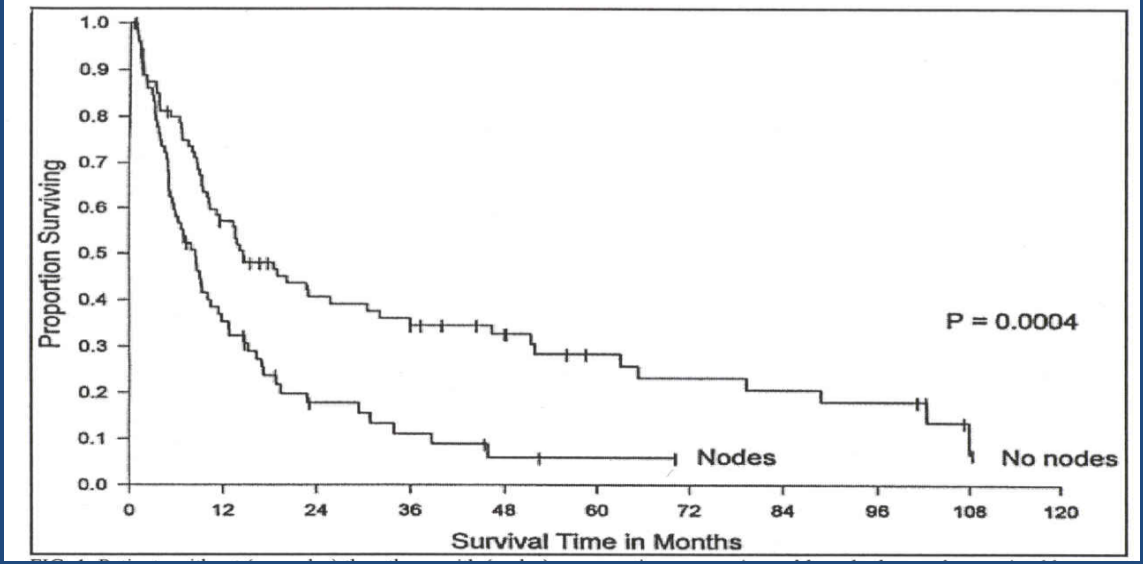
LND in Metastatic RCC

- 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

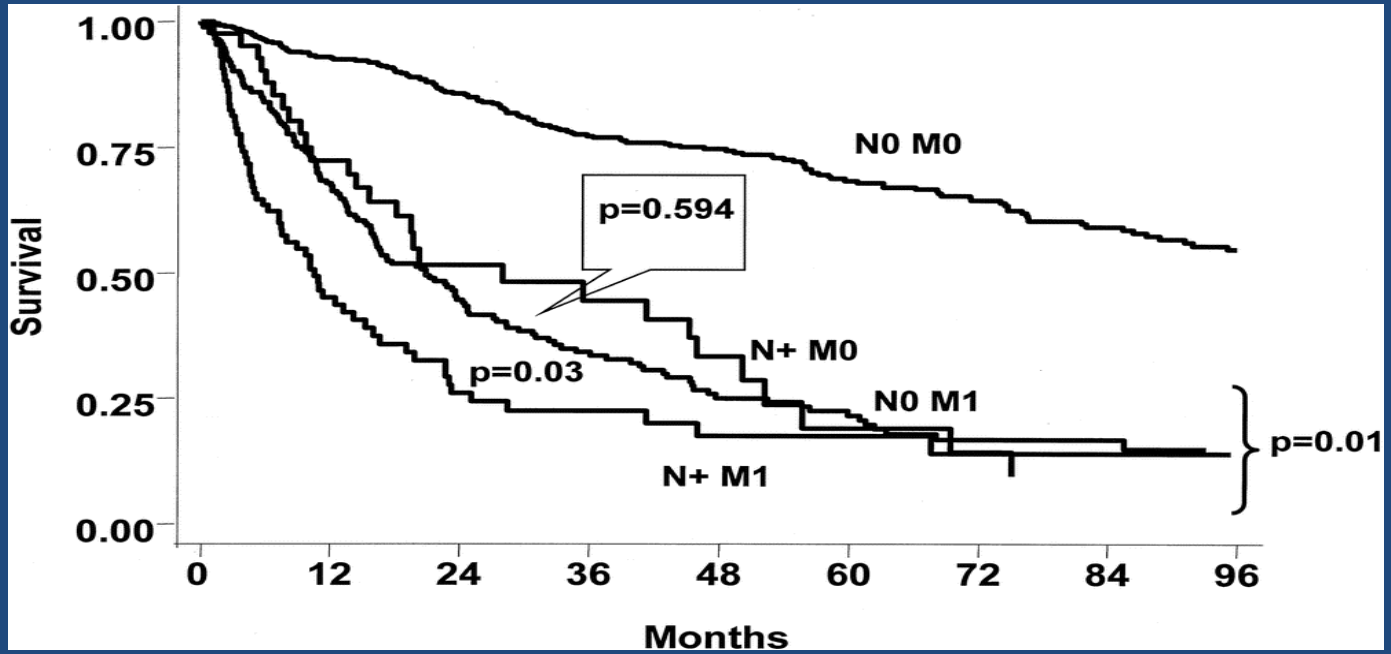


Survival

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

Vasselli et al. J Urol., 2001

Overall Survival for RCC Patients With and Without Nodal Metastases



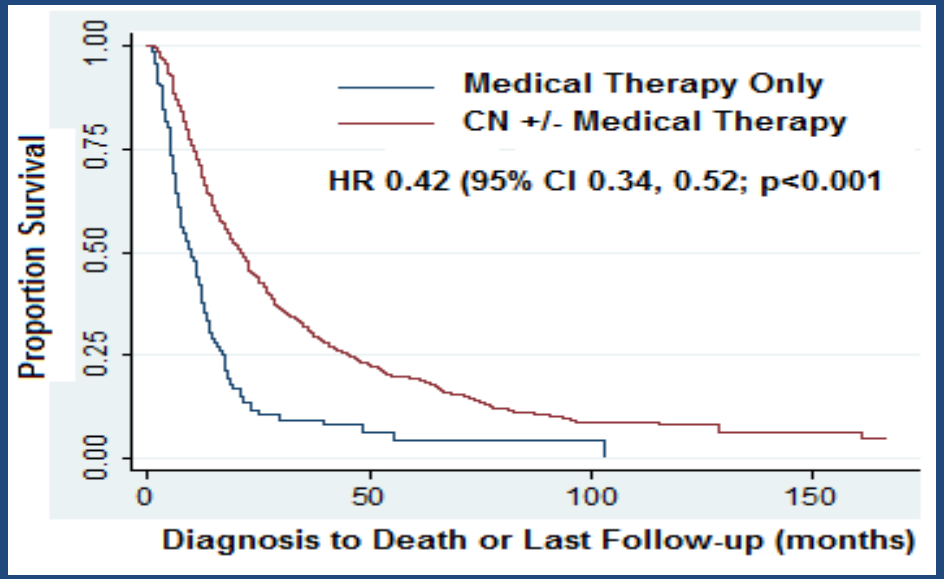
Pantuck *et al.*, J Urol, 2003

Identifying Patients who will Not Benefit from Cytoreductive Nephrectomy: MDACC

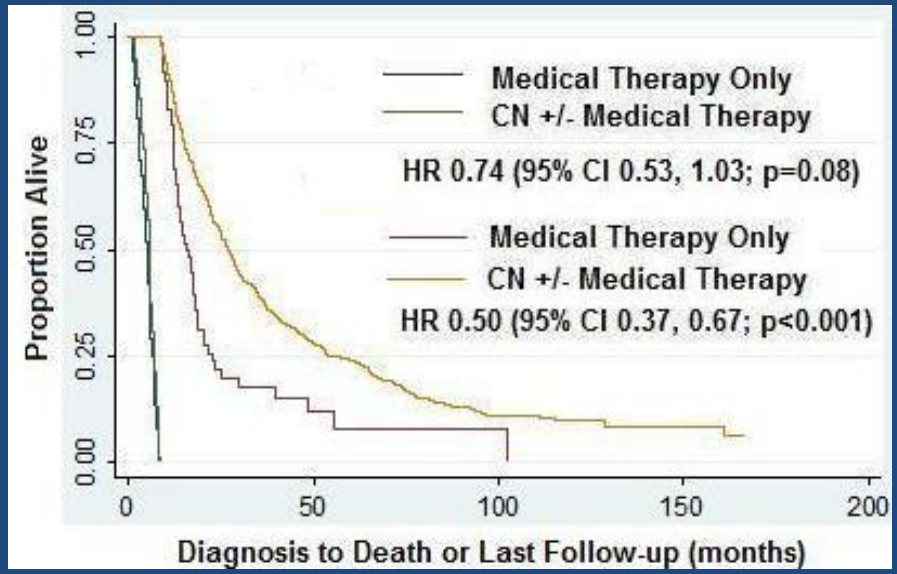
- 566 pts undergoing CN between 1991 and 2007
- 110 pts undergoing medical therapy only
- Compared survival between groups and identified when survival diverged between surgical and non-surgical groups
- Identified pre-operative variables that differed between surgical groups based on follow-up
- Pre-operative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

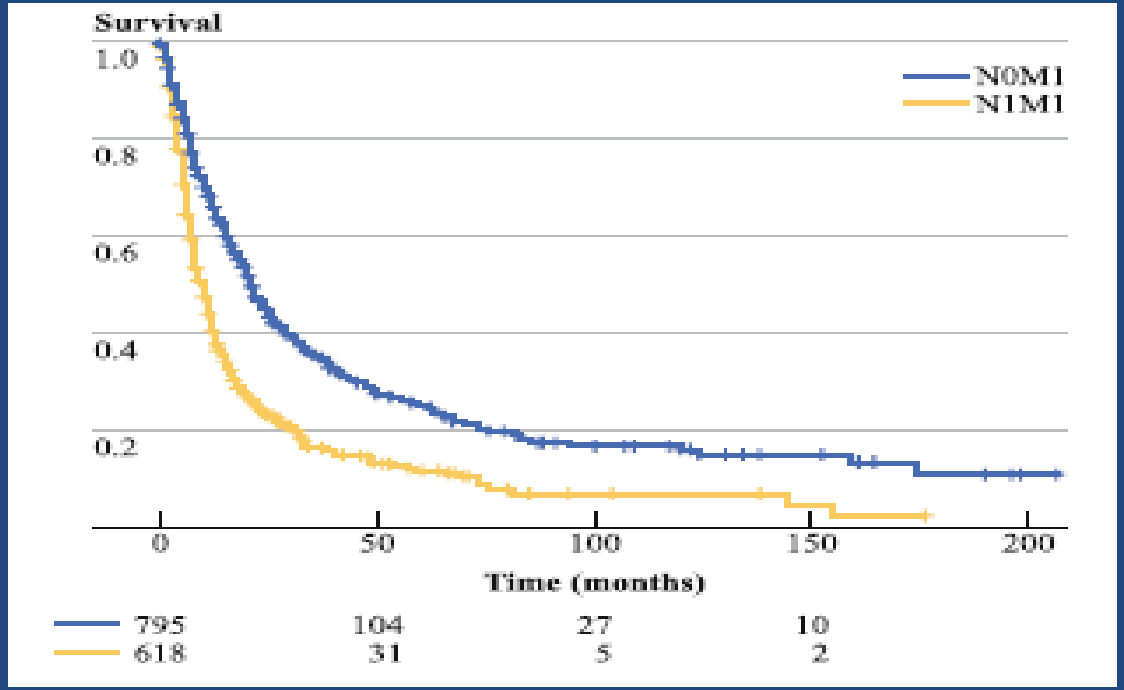
Culp et al., Cancer, 2010

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

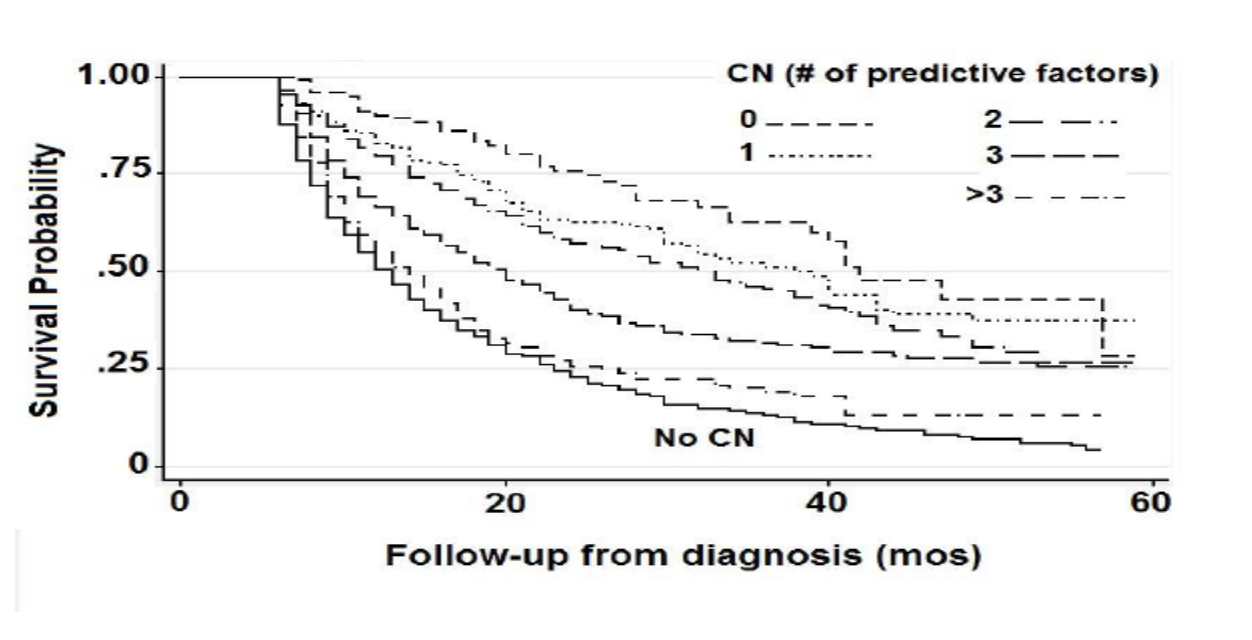
Culp et al., Cancer, 2010

The Presence of Nodal Metastases Predicts Outcome in mRCC



Trinh QD et al, Ann Surg Onc, 2012

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



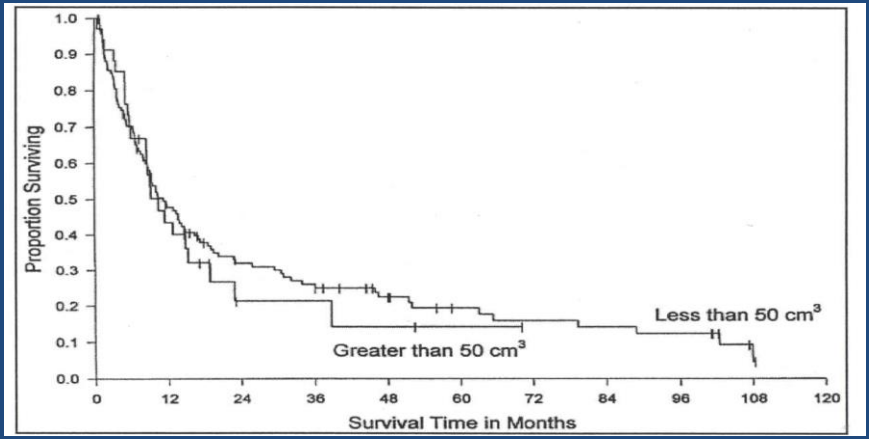
Predictive Clinical Factors

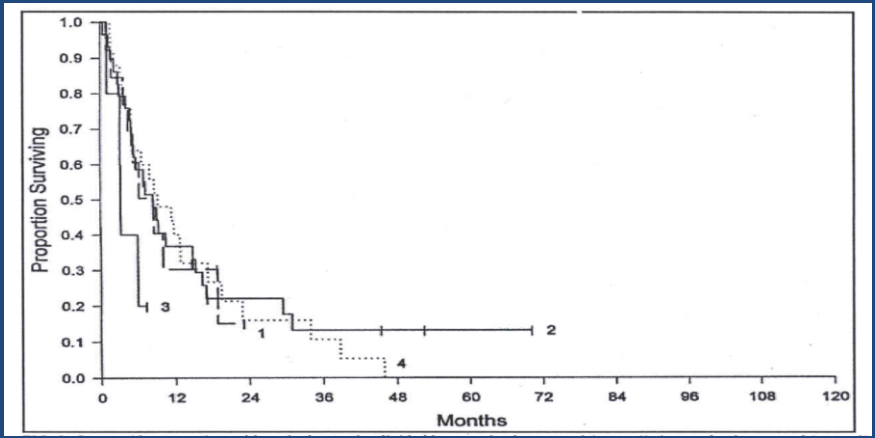
1. Size > 7 cm
2. cT3 or cT4 Stage
3. High grade (3 or 4)
4. Positive lymph nodes
5. Sarcomatoid Histology

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 cm^3 : 10.5

> 50 cm^3 : 5.3

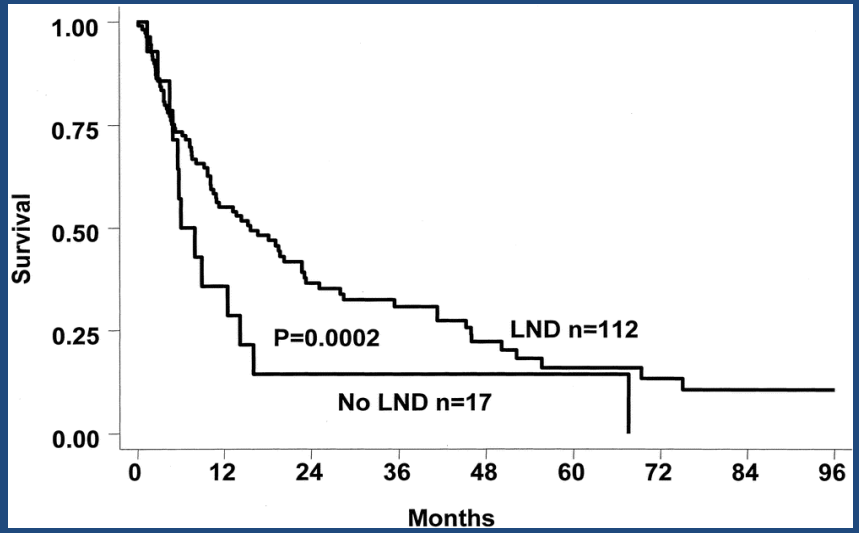
Survival (mos)

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)

Vasselli *et al*. J Urol., 2001

Importance of LN Dissection in Renal Carcinoma



Clinical Evidence Of Nodal Metastases

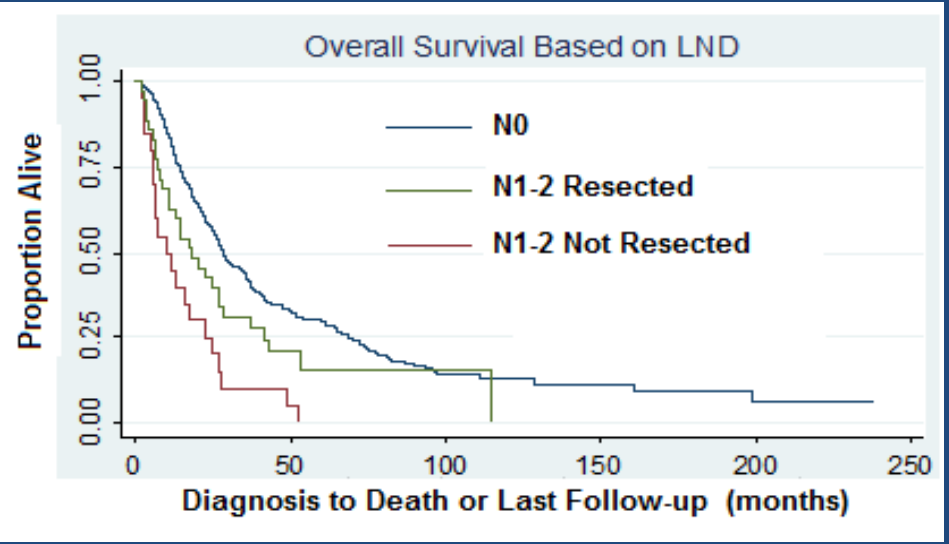
*No difference in RFS, M status not specified

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 - $T_{any}N_0M_1$
- 55 - $T_{any}N_{1-2}M_1$
- Clear cell histology
- Retroperitoneal adenopathy only

	Hazard Ratio (95% CI)	P	Median Survival (mos)
N_0M_1	Referent	--	28.4
$N_{1-2}M_1$ + LND	**1.53** (1.04, 2.25)	0.03	18.3
$N_{1-2}M_1$ <u>No</u> LND	**3.10** (1.95, 4.91)	<0.001	9.8



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?

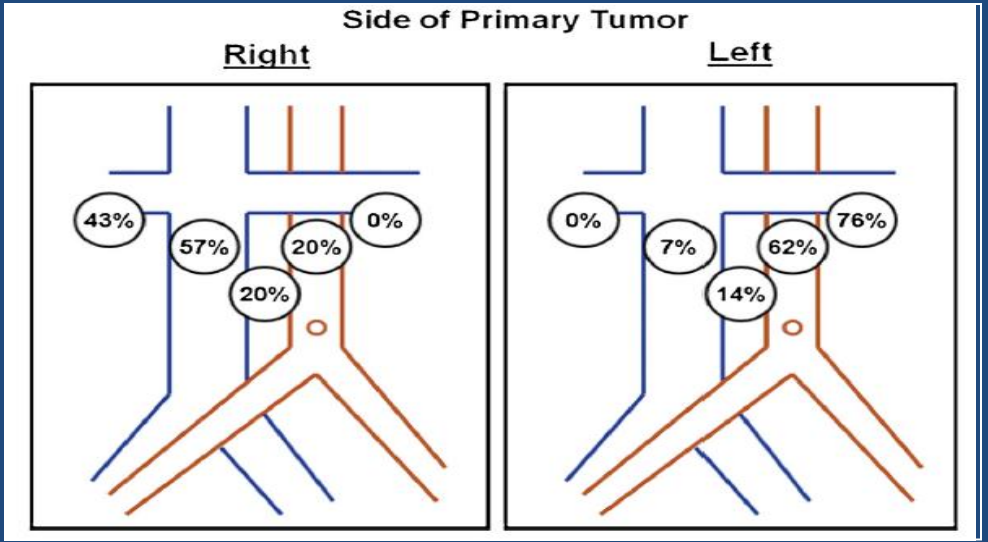
European Association of Urology

Kidney Cancer

Lymph Node Dissection at the Time of Radical Nephrectomy for High-Risk Clear Cell Renal Cell Carcinoma: Indications and Recommendations for Surgical Templates

Paul L. Crispen[a], Rodney H. Breau[a], Cristine Allmer[b], Christine M. Lohse[b], John C. Cheville[c], Bradley C. Leibovich[a], Michael L. Blute[a,]*

- 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.



Location of +LN based on side of primary tumor. Percentage represents frequency of involved location in patients with lymph node–positive disease.

EORTC 30881

Table 3 – Complications of surgery in eligible patients

	Without lymph-node dissection ($n = 370$)		With complete lymph node dissection ($n = 362$)	
	n	%	n	%
Bleeding >1 l	24	6.5	34	9.4
Pleural damage	19	5.1	16	4.4
Infection	21	5.7	19	5.2
Bowel damage	5	1.4	2	0.6
Embolism	4	1.1	8	2.2
Lymph fluid drainage	9	2.4	14	3.9
Total	82		93	

Blom JH et al., Eur Urol, 2009

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?”