“Ode to a node”
Lymph node dissection in prostate and bladder cancer

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Introduction – prostate cancer

- PLND most accurate and reliable staging method for LNI
- Imaging techniques have limited ability to detect LNI
- Nomograms have an apparent high accuracy (76-97.8%) but underestimate LNI
- NB No RCT data exists

Patient selection – LNI Rate

- Low risk CaP patients rate of LNI low
- Largest series from Makarov
  - 2896 patients T1c, PSA <6
  - LNI was 0.7%
- Most recent update to Partin’s tables
  - 5730 patients T1c, PSA <10, Gleason ≤6
  - LNI <1%
- ePLND in low risk patients
  - 474 low risk CaP patients
  - LNI 7.4%
- Range of LNI across published data is 0.5-0.7% with IPLND and does not exceed 8% with ePLND
### Guidelines

<table>
<thead>
<tr>
<th>Organization</th>
<th>Indication for PLND</th>
<th>Extent of PLND</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Association of Urology</td>
<td>Men with intermediate PSA 10-20 ng/ml, biopsy</td>
<td>Extended</td>
</tr>
<tr>
<td></td>
<td>Gleason score 7 or high risk (&lt;70, PSA &gt;20 ng/ml)</td>
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<tr>
<td>American Urological Association</td>
<td>PLND generally reserved for patients with higher risk of nodal involvement</td>
<td>Not Indicated</td>
</tr>
<tr>
<td>National Comprehensive Cancer</td>
<td>PLND can be excluded in patients with &lt;7% predicted probability of lymph node</td>
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<tr>
<td>Network</td>
<td>metastases by nomograms, although some patients with nodal metastases will be</td>
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<tr>
<td></td>
<td>missed. An extended PLND is preferred when PLND is performed.</td>
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</table>

*PLND = pelvic lymph node dissection; PSA = prostate-specific antigen.*

### Anatomy and extent of PLND

![Anatomy and extent of PLND](image)

1. External iliac and obturator
2. Internal iliac
3. Presacral and perirectal
4. Common iliac
5. Paraaortic/caval
6. Inguinal
ePLND vs IPLND

- 123 patients randomised to IPLND vs ePLND
- No difference in LNI (3.2% vs 4%)
- Criticisms:
  - Low risk patients
  - Unilateral ePLND
  - ePLND boundaries not defined
  - Underpowered
Anatomy and extent of PLND

- CaP metz do not follow a predefined pathway of spread
- Removal of LN’s from obturator fossa and external iliac vessels under-estimates LNI
- 50% of LN metz are located along hypogastric artery
- Most extensive PLND 25% of LN’s potentially involved would not be removed

Effect on survival

<table>
<thead>
<tr>
<th>Study</th>
<th>No. Of Patients</th>
<th>Result</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Masterson et al (2006)</td>
<td>4611</td>
<td>Inverse association between number of nodes removed and bPFS in node negative patients</td>
<td>? removal of micrometastatic disease</td>
</tr>
<tr>
<td>Joslyn et al (2006)</td>
<td>13020</td>
<td>Removal of 4 LNs (all patients) &gt; 10 nodes (N-) had a lower risk of prostate cancer-specific death at 10 years</td>
<td>PLND could improve CSS in the long term? removal of micrometastatic disease</td>
</tr>
<tr>
<td>DiMarco et al (2005)</td>
<td>7036 T1-T3, N0</td>
<td>No. Of LNs removed over the 13 year period decreased No. of LNs obtained at PLND not associated with PSA progression</td>
<td>Extent of LND does not affect CaP outcomes Under staging not present in N- cases with IPLND (even if present, its impact appears negligible)</td>
</tr>
<tr>
<td>Murphy et al (2010)</td>
<td>964 T2-T4, N0</td>
<td>preopPSA, pGleason score, path stage, margin status predictors of biochem recurrence LN yield not a predictor for biochem recurrence</td>
<td>Higher LN yield does not increase the chance of cure for patients overall or when stratified into risk groups</td>
</tr>
</tbody>
</table>
Outcome for patients with LNI

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients</th>
<th>Cancer specific survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boorjan et al (2007) J Urol</td>
<td>505</td>
<td>85% (10 years)</td>
</tr>
<tr>
<td>Schumacher et al (2008) Eur Urol</td>
<td>122</td>
<td>60% (10 years) ≤2 or ≥3 positive nodes removed, CSS at 10 years was 78.6% and 33.4%</td>
</tr>
<tr>
<td>Briganti et al (2009) Eur Urol</td>
<td>703 (NB Multimodal approach)</td>
<td>78% (15 years) ≤2 or ≥3 positive nodes removed, CSS at 15 years 84% vs 62%</td>
</tr>
</tbody>
</table>

- NB. Volume of nodal disease is an important predictor of outcome

Treatment of N+ patients

- Controversial
- Immediate vs deferred ADT?
    - Randomised 47 patients to immediate ADT and 51 to observation
  - Immediate ADT significant improvement in OS, CSS and bPFS
- Adjuvant RT?
  - DaPozzo et al (2009)
  - Retrospective study
  - 129 patients were treated with RT and ADT, while 121 ADT alone
  - CSS 10 years 41.7% ADT alone vs 51% RT plus ADT
Conclusions

- Lack of robust data
- Rate of LNI in low risk CaP patients is low
- IPLND underestimates LNI
- If performed it should be extended
- Effect on outcome remains unclear
- Randomised prospective data required to assess the long-term outcome of ePLND
Introduction – PLND Bladder cancer

- 20 – 40% of muscle invasive disease
- Nearly 25% have pathological evidence of LN metz at RC
- LN metz most important prognostic variable in determining outcome following RC
- Rationale based on natural Hx of disease
- Imaging techniques have limited ability to detect LNI

Stein (2001) J Clin Oncol
Anatomy and extent of LND

• 1° drainage obturator nodes, then the internal and external iliac nodes (pelvic nodes)
• 2° and 3° drainage is to the common iliac (CI), para-caval and para-aortic nodes
• Direct drainage to pre-sacral nodes from the trigone and posterior bladder wall
• LN metz contralateral to 1° site is common (>40%)
• Metz to CI and proximal nodes in the absence of pelvic metz is uncommon
• Presacral only nodal metz extremely rare (1% to 3%) without lower level nodal involvement

Anatomy and extent of LND – surgical boundaries

• Boundaries of an “extended” LND
  – Proximal: aortic bifurcation and CI vessels
  – Lateral: genitofemoral nerve
  – Distal: circumflex iliac vein and Cloquet node
  – Posterior: hypogastric vessels including the obturator fossa and presacral nodes
• NB Extended dissections may extend to IMA
Anatomy and extent of LND – surgical boundaries

• Boundaries of a “standard” lymphadenectomy cephalad
  – Proximal: CI bifurcation
  – Lateral: genitofemoral nerve
  – Distal: circumflex iliac vein and Cloquet node

• NB presacral nodes not removed

Anatomy and extent of LND - Location of LN metz

<table>
<thead>
<tr>
<th>Study</th>
<th>No. Of Patients</th>
<th>Technique</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leisner 2004 J Urol</td>
<td>290</td>
<td>ELND to IMA</td>
<td>74% of LN metz left behind and 7% understaged as N0 with sLND NB 8% presacral, 16% above aortic bifurcation</td>
</tr>
<tr>
<td>Abol-Enein 2004 J Urol</td>
<td>200</td>
<td>ELND to IMA</td>
<td>13% above aortic bifurcation There were no skip lesions - Negative nodes in the endopelvic region indicate that more proximal dissection is not necessary</td>
</tr>
<tr>
<td>Vazina 2004 J Urol</td>
<td>176</td>
<td>ELND to IMA</td>
<td>5.1% presacral, 4% above aortic bifurcation 33% with CI involvement had involvement of presacral nodes</td>
</tr>
<tr>
<td>El-Shazli 2004 J Egypt Natl Canc Inst.</td>
<td>109</td>
<td>ELND to IMA</td>
<td>34.4% LN metz above aortic bifurcation</td>
</tr>
</tbody>
</table>
Anatomy and extent of LND – location of LN metz

- Should perform extended over standard
- How extended? debatable

Effect on survival

- Prognosis of pelvic recurrence after RC is poor
- SEER data: Only 40% have a LND
- Kerr and Colby first suggested the potential benefit of a PLND in 1950
- Skinner proposed in 1982 that “a meticulous pelvic node dissection can make a difference”
- No RCT demonstrated differences in survival ± LND, strong evidence supporting some form of LND
Effect on survival

• Leissner et al 2000 retrospective
  – 447 patients undergoing RC
  – eLND improves survival for LN- and LN+, with reduced local recurrence rate when a greater number of LNs (16) were removed
• Poulson et al 1998 retrospective
  – 194 patients; 126 eLND, 68 sLND
  – 5-yr recurrence-free survival rate in organ-confined N- 90% eLND vs 71% in sLND group
  – NB ePLND reduced the pelvic and distant metastases rate in these patients

Effect on survival

• Grossman et al 2003 RCT
  – 270 underwent RC; 24 no LND, 98 obturator only, 146 sPLND
  – 5-year survival rates: 33%, 46%, and 60%, respectively
  – Survival rate with <10 LNs removed was significantly lower than patients with >10 LNs removed (44% vs. 61%, respectively)
Effect on survival

- Dhar et al 2008 Retrospective
  - ILND (336 cleveland clinic) and eLND(322 Bern)
  - All cases were N0 M0

- The 5-yr recurrence-free survival rate:
  - LN+ disease 7% vs 35% ILND vs eLND.
  - pT2 pN0 67% vs 77% ILND vs eLND
  - pT3 pN0 23% vs 57%

Morbidity and Mortality

- Broesner 2004
  - 46 patients eLND vs 46 patients ILND
  - No difference between groups

- Poulsen 1998
  - No difference in mortality, lymphocele formation

- Leissner 2000, 2004
  - Lymphoceles and lymphoedema 2% >16 nodes, 1% <16 nodes
  - No centres found any significant adverse effects with eLND
Conclusions

• Extended PLND allows for more accurate staging and possibly the removal of undetected micrometastases
• This could improve survival of patients with histopathologic N+ and N- disease
• Definitions !!
• Results from the German randomized multicenter study comparing an extended PLND versus limited PLND along with cystectomy are awaited

Questions