Completion Node Dissection for Sentinel Node Positive Melanoma is OVERRATED

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Grand Rounds
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Overview

• Background
  – Elective lymph node dissection (ELND) to Sentinel lymph node dissection (SLND)
  – MSLT- I

• MSLT- II

• Melanoma patients with positive SLN and NSN

• Studies comparing SLN positive patients not undergoing CLND

• Morbidity of CLND

• Conclusions
Evolution of ELND to SLND

• ELND was the standard of care in 1970’s

• Large randomized controlled trials demonstrated no overall survival with ELND

SLND and the MSLT-I

• 1992 first published report of SLND in melanoma
• 1994 Morton et al., opened the MSLT-1; results published in 2006.
• 1999: World Health Organization declares SLNB standard of care

MSLT-I

- ~2000 patients randomized from 1994-2001
- ~1300 patients had melanoma 1.2-3.5 mm described in NEJM
Important Findings

A. Disease-free Survival

B. Melanoma-specific Survival

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Observation group</th>
<th>Biopsy group</th>
</tr>
</thead>
<tbody>
<tr>
<td>500</td>
<td>393</td>
<td>290</td>
</tr>
<tr>
<td>454</td>
<td>236</td>
<td>146</td>
</tr>
<tr>
<td>62</td>
<td>99</td>
<td>8</td>
</tr>
</tbody>
</table>

C. Disease-free Survival

D. Melanoma-specific Survival

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Sentinel-node-negative subgroup</th>
<th>Sentinel-node-positive subgroup</th>
</tr>
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<tbody>
<tr>
<td>642</td>
<td>566</td>
<td>406</td>
</tr>
<tr>
<td>406</td>
<td>204</td>
<td>87</td>
</tr>
<tr>
<td>87</td>
<td>6</td>
<td>6</td>
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<td>122</td>
<td>85</td>
<td>50</td>
</tr>
<tr>
<td>85</td>
<td>31</td>
<td>12</td>
</tr>
<tr>
<td>31</td>
<td>12</td>
<td>2</td>
</tr>
</tbody>
</table>

P-values:
- P=0.009
- P=0.58
- P<0.001
- P<0.001
MSLT-I Conclusions

• SLN biopsy
  – Provides important staging and prognostic information
  – Improves disease free survival
  – Did not demonstrate improved melanoma specific survival/overall survival
**Biopsy-Proven Melanoma**

- **LM/SNB**

  - Identification of SN Metastases by H&E/IHC or by RT-PCR

  - **Stratification** *(Breslow, ulceration, size of SN metastases)*

  - **Randomize**

    - **CLND**
      - Observation
    - **Serial Ultrasonography of LM/SNB Basin**
      - **Nodal Recurrence**
      - **CLND**
Dr. Donald L. Morton, MD

BA: UC Berkley

MD: UCSF

Surgical Residency: UCSF

Oncology Fellowship: UCSF

Established John Wayne Cancer Institute at St. John’s Health Center in Santa Monica, CA

Pioneered SNB in Melanoma

Over 600 Peer Reviewed Publications

Melanoma Survivor
What is the Prevalence of Positive SLN?

• Most published studies report 15-25%

• MSLT-I
  – 16% of patients had positive SLN
What is the Prevalence of Additional nodes with Positive SLN?

15-20%
Factors Predictive of Tumor-Positive Nonsentinel Lymph Nodes After Tumor-Positive Sentinel Lymph Node Dissection for Melanoma

Jonathan H. Lee, Richard Essner, Hitoe Torisu-Itakura, Leslie Wanek, Hejing Wang, and Donald L. Morton

John Wayne Cancer Institute; 2004
Retrospective Review
1,500 pts SLND; 20% CLND

25% patients with +SLN had +NSN……75% DID NOT have additional + NSN!!
Factors Predictive of Tumor-Positive Nonsentinel Lymph Nodes After Tumor-Positive Sentinel Lymph Node Dissection for Melanoma

Jonathan H. Lee, Richard Essner, Hitoe Torisu-Itakura, Leslie Wanek, Heijing Wang, and Donald L. Morton

John Wayne Cancer Institute; 2004
Retrospective Review 1500 pts

75% patients DO NOT have +NSN
400 patients with SLN positive disease

17% patients had positive NSN
  – 65% had ONE positive NSN
What about Survival and CLND?
Survival

- Recall only 20% of patients with melanoma have positive SLN
- Patients with positive SLN, only 25% will have positive NSN

- 100 patients with melanoma
  - 15 patients undergoing unnecessary CLND
  - 5 patients may benefit….but 65% have ONE positive NSN
Melanoma Patients with Positive Sentinel Nodes Who Did Not Undergo Completion Lymphadenectomy: A Multi-Institutional Study

- 16 centers with 134 patients with positive SLN did not have CLND
- Cohort 164 MSKCC patients with positive SLN followed by CLND
- Primary endpoints: Recurrence and Disease Specific Survival
“Disease specific survival with positive SLN patients who did not undergo CLND was 80% at 36 months…. NOT significantly different from that of patients who underwent CLND”
• 15% patients who did not undergo CLND had nodal recurrence
• Median time to recurrence was 11 months
• 15%......Remember most studies quote ~20% positive NSN after CLND
• ID’s patients who really need CLND
• Retrospective Review 1200 patients

• Compared 5 year overall survival SLN +/-CLND vs. FN SLN

  – FN: initial negative SLN biopsy with later nodal disease in absence of local or in transit recurrence

Poland; 2006
• Results:
  – FN rate 5%
  – Median time to detection of nodes in FN group: 16 months (3-74 months)
  – FN group higher ratio of 2 or more + NSN
  – Overall 5 year survival
    • FN 53.7% vs CLND 56.8% (p =0.9)
Completion Node Dissection in Patients with Sentinel Node–Positive Melanoma of the Head and Neck

Valerie A. Smith¹, Joan E. Cunningham, PhD², and Eric J. Lentsch, MD³

SLNB  
\[ n = 4,477 \]

SLN positive  
\[ n = 400 \]

SLNB only  
\[ (\leq 5 \text{ LN removed}) \]  
\[ n = 140 \]

SLNB + CLND  
\[ (\geq 10 \text{ LN removed}) \]  
\[ n = 210 \]

University of South Carolina; 2012 Retrospective Review
Conclusions: “The cohort as a whole DID NOT significantly benefit from CLND…. Compared with SLNB alone, CLND DOES NOT seem to be associated with improved survival.”
## Morbidity with CLND

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No.</th>
<th>Wound Separation</th>
<th>Seroma/Hematoma</th>
<th>Infection</th>
<th>Total*</th>
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<tbody>
<tr>
<td>LM/SNB</td>
<td>937</td>
<td>11 (1.2%)</td>
<td>52 (5.5%)</td>
<td>43 (4.6%)</td>
<td>95 (10.1%)</td>
</tr>
<tr>
<td>LM/SNB + CLND</td>
<td>234</td>
<td>7 (3.0%)</td>
<td>54 (23.1%)</td>
<td>37 (15.8%)</td>
<td>87 (37.2%)</td>
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Conclusions

- SLND provides important staging and prognostic information
- SLN positive ~20%, prevents unnecessary lymph node dissection
- Patients with positive SLN, only 20% have NSN positive nodes
- 65% of patients w NSN have only one positive node
- Overall survival not significantly different in patients with positive SLN who did not have CLND
- With time, patients with positive NSN will present with recurrence in nodal basin
- Significant morbidity associated with CLND
- Results of MSLT-II will provide valuable information and may change the management of lymph node dissection
“And Now You Know the Rest of the Story!”

(Paul Harvey)