Sentinel Lymph Node Detection in Cervical Cancer

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Introduction

cervical cancer metastasize mainly lymphatic

lymph node status is the most important prognostic factor

lymphadenectomy - gold standard

If lymph node metastases are present at the time of primary surgery

5-year survival drops from 85% to 50%.
Lymphadenectomy may be associated with remarkable side effects:

- vessel injuries, nerve affection
- lymph cysts
- lymph edema.

Development of laparoscopy results in new techniques
- LARVH with pelvic +/- paraaortic lymphadenectomy*
- SENTINEL CONCEPT
to reduce morbidity of the surgical approach.

**Introduction**

**Aim/Study**

-evaluation of detection rate and diagnostic accuracy of sentinel lymph node technique (sensitivity and NPV)
- patients with cervical cancer
- all stages
Tracer application

Tc-albumines
60 MBq the day prior (1ml)
or
10 MBq the day of surgery

Blue dye
4 ml after anesthesia
laparoscopic pelvic lymphadenectomy (left)

surgical procedure

laparoscopic paraaortic lymphadenectomy

Results

December 1998-October 2006
507 patients for analysis of accuracy
median age 41 years (range 16-79 years)

FIGO stage
- IA1 in 38 patients
- IA2 in 42 patients
- IB1 in 265 patients
- IB2 in 55 patients (10.8%)
- IIA or IIB in 91 patients (17.9%)
- IIIA to IVB in 15 patients (3%)

68%
# Results

## Identification of Sentinel Lymph Nodes

<table>
<thead>
<tr>
<th>Description</th>
<th>Detection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over all</td>
<td>90% (CI95 86.9-92%)</td>
</tr>
<tr>
<td>Pelvic</td>
<td>89% (CI95 85.8-91.1%)</td>
</tr>
<tr>
<td>Tc alone (n=55)</td>
<td>82% detection rate</td>
</tr>
<tr>
<td>Blue dye alone (n=195)</td>
<td>82% detection rate</td>
</tr>
<tr>
<td>Tc+Blue dye (n=340)</td>
<td><strong>94%</strong> detection rate <em>(p&lt;0.001)</em></td>
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</table>

## Accuracy of Diagnostic Test

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
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<tbody>
<tr>
<td>Pelvic lymph node metastasis</td>
<td>n=106 patients</td>
</tr>
<tr>
<td>Sentinel lymph nodes correctly predict metastatic disease</td>
<td>n=82 patients</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>77% (CI 68.2-85%) <em>(&lt;90% of clinically acceptability)</em></td>
</tr>
<tr>
<td>NPV</td>
<td>94% (CI 83-99.4%)</td>
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</table>
Results

Identification of sentinel lymph nodes

tumor size

tumor ≤20mm in 249 patients (45.8%)
tumor >20mm in 305 patients (47.7%)
(6.5% no data)

overall detection rate

94% in tumor ≤20mm
84% in tumor >20mm (p<0.001)

Results

Accuracy of diagnostic test

tumor size

sensitivity

≤ 20mm = 91% (70.8–98.9%)
>20mm = 72.7% (61.3–82.3%)
(p=0.091)

NPV

≤ 20mm = 99% (96.6 – 100%)
>20mm = 88.5% (82.9 – 92.8%)
(p<0.001)
Probability of diagnostic outcome in all patients – flowchart-

SLN: Pelvic SLN (Index test)
Reference: Pelvic nodal status

Probability of diagnostic outcome in patients with cervical cancer ≤20mm – flowchart-

SLN: Pelvic SLN (Index test)
Reference: Pelvic nodal status
In our cohort of patients (n=507) with cervical cancer of all stages the sensitivity of the sentinel concept was clinically unacceptable.

Encouraging data were obtained for 249 patients with tumors smaller than 21mm diameter in this study.

Is the procedure safe when ≥1 SLN can be detected bilaterally and the cervical specimen includes 50% of the parametrium with the inner parametrial LN at risk?

This should be confirmed in further trails.
SLN

Review of literature

Summary

Authors: n=21
Years: 2000-2007
Number of patients: 20-100 831
SLN indentified: 70-100% 90%
Sensitivity: 63-100% 92%
False negative: 0-38% 8,2%
NPV: 88-100% 97,3%

Conclusion

„Missing nodal disease 8% of the time might too high for gynecologic oncologist to accept as the decision to administer adjuvant therapy may be made solely on the knowledge of nodal status."

„Ten percent is probably to high to be acceptable false-negative rate…. but what is acceptable?“

…5% …3% ??
SLN


Conclusion

- SLN technique is applicable
- Further clarification is needed

? tolerable false negative rate
? role of isolated micrometastatic disease

Micrometastasis in SLN

Horn et al., Gynecol Oncol: 111 (2008) 276–281

Prognostic impact of micrometastases (<2mm) in pelvic lymph nodes in patients with cervical cancer FIGO stage IB-IIB.

n= 894 patients

pN1 = 281 patients (31.4%)
pN1 mic = 59 patients (22.2%), obturator and internal nodes were affected

pN1 mic RFS-rate at 5-years = 68.9% (pN0=82.4%)
pN1 mic OS-rate at 5-years = 63.8% (pN0=86.6%)
Conclusion

“Micrometastatic disease represents an independent prognostic factor. So, all patients with pelvic lymph node involvement, including micrometastatic deposits, might be candidates for adjuvant treatment.”

SLN technique is helpful to identify affected nodes!

Micrometastasis in SLN


Intraoperative (imprint cytology and frozen section) versus postoperative assessment of SLN in early cervical cancer.

N=38 patients (FIGO IIA-IIB)
Primary tumor size <2cm =21 (55.3%)
>2cm =17 (44.7%)
SLN detection rate =92%

pN1=6 patients (15.7%), macro=2, micro=2, ITC=2
Intraoperative evaluation correctly identified lymph node metastasis in only 33.3%.
Conclusion

“However, while current intraoperative pathology techniques for assessing nodal metastases reliably detect metastases larger than 2 mm, they lack sufficient sensitivity to detect micrometastasis and isolated tumor cells.”

Questions

1. What is a acceptable false negative rate?

2. What is the role of micrometastasis detected in parametrial and pelvic SLN? - adjuvant treatment?

3. How save is the intraoperative histopathological assessment of SLN?

4. What is our SLN – standard? i.e.
- combined application of radiocolloid and blue dye
- bilateral detection is needed
- lymphoscintigraphy and/or SPECT-CT
Conclusion

Looking at the literature sentinel lymph node biopsie alone is currently not a routine procedure for staging of cervical cancer patients.

SLN-standards are needed for application, detection, and histopathological evaluation.

The oncologic safety of the SLN technique for tumors <2cm should be confirmed in further trails.

Thank you for your attention!