Dose-volume effects in pathologic lymph nodes in cervical cancer


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BACKGROUND

• For locally-advanced cervical cancers, excellent local control rates with primary tumor dose $\geq 85\text{Gy}$
• Nodal boost in node-positive disease
  • The dose threshold remains unclear.

PURPOSE

• To identify a treatment planning objective for pathologic nodes in cervical cancer
• To identify factors of nodal control
• To describe patterns of failure among node-positive cervical cancer patients
METHODOLOGY

Case selection

- Retrospective (2002-2011)
- Node-positive, non-metastatic* cervical carcinoma
- Treated curatively with chemoradiation and image-guided adaptive brachytherapy (IGABT)
- No prior hysterectomy

Nodal staging

- Abdominopelvic CT and pelvic MRI
- PET-CT
- Para-aortic lymph node dissection (PALND)*
METHODOLOGY

Treatment

• Chemoradiation: conformal, 45-46Gy with concurrent cisplatin

• PDR - IGABT: $CTV_{HR} D_{90} \geq 85\text{Gy}; CTV_{IR} D_{90} \geq 60\text{Gy}$ using personalized vaginal molds

• ±Nodal boost: cumulative dose 60Gy, given sequentially or as simultaneous integrated boost

Prognostic factors for nodal control

• Nodal volume, dose, histology, concurrent chemotherapy, simultaneous boost

• Univariate analysis (log-rank tests), multivariate analysis (Cox proportional model; factors with $p \leq 0.10$ in univariate)

• Probit analyses

• XLSTAT 2014
RESULTS

**Disease characteristics**

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<th>Eligible cases, 108</th>
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<th>Lymphadenopathies, 252:</th>
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<td>(para-aortic, 19 pelvic, 233, inguinal, 2)</td>
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**T stage**
- T1b/T2a, 35%
- **T2b, 43%; T3b, 15%**

**Tumor size**
- ≤5cm 44%
- >5cm 56%

- **Squamous cell carcinoma, 61%**
- Grade 2-3, 59%
- Volume 3.4cm$^3$ ±5.8
- Cumulative EQD2 55.3Gy ±5.6
RESULTS

Treatment characteristics

Eligible cases, 108

Lymphadenopathies, 254:
- Para-aortic, 19
- Pelvic, 233
- Inguinal, 2

Staging
- CT, 100%
- MRI, 100%
- PET-CT, 94.4%

Treatment
- 45.1 ±1.1Gy
- Conformal, 85%
- Chemotherapy, 96%
- Intracavitary brachytherapy, 96%, interstitial, 4%
- Nodal boost, 67% (sequential, 84%; simultaneous 16%)

Under peer review
RESULTS

Patterns of failure (n=41)

Median follow-up: 33.5 months (3-138 months)

Initially involved nodes, 254

Nodal failures, 86
(23 in initially pathologic nodes)

Presacral, 4; parametrical, 3; perirectal, 2;
inguinal, 2

Presacral, 1 (0); inguinal, 4 (0)
RESULTS

Prognostic factors for nodal control

- Univariate analysis
  - Volume (≥3 cm³, p<0.0001)
  - EQD2 (≥57.5Gy, p=0.039)
  - SIB (p=0.07)
  - Histology (SCC versus others, p=0.35)
  - Chemotherapy (p=0.39)

- Multivariate analysis
  - Volume (HR=8.2, 4.0-16.6, p<0.0001)
  - EQD2 (HR=2, 1.05-3.9, p=0.034)
CONCLUSION

• In node-positive disease, distant metastasis is the most common form of failure.

• Nodal failure, however, remains significant despite excellent local control.
  • Poorer control with nodal volumes $\geq 3$cc
  • Better control with nodal EQD2 $\geq 57.5$Gy

• A nodal dose-volume control relationship is demonstrated.