Rates, Determinants, and Outcomes of Radical Prostatectomy in Prostate Cancer Patients with Clinical Node-Positive Disease

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BACKGROUND

• Current consensus (NCCN) guidelines recommend that prostate cancer (PCa) patients with "regional risk" clinical node positive (cN1) disease undergo external beam radiation therapy (EBRT) and ADT.
• However, the role of clinical node status in predicting benefit from radical prostatectomy (RP) is debated, and the majority of cN1 patients undergo RP.

Our objectives were to:
1. Characterize the rates and determinants of initial RP for patients with cN1 disease
2. Assess the prognostic significance of clinical nodal stage for patients who undergo RP and have pathologic node involvement (pN1)

METHODS

• We identified two cohorts of incident cases of non-metastatic (M0) PCa within the National Cancer Database (NCDB) from 2004-2016.
  (1) cN1 cohort: Patients with cN1 disease
  (2) pN1 cohort: Patients with pN1 disease on RP
• cN1 cohort: Factors associated with receipt of initial RP were identified using multivariable risk difference regression. Post-surgical pathologic staging and adjuvant therapies were described for cN1 patients undergoing RP.
• pN1 cohort: Multivariable Cox regression and the log rank test were used to compare overall survival (OS) by preoperative clinical stage (cN1 vs cN0).

RESULTS

• Overall, 27% (N=3079) of patients with cN1 disease underwent initial RP.
• Annual rates of initial RP for cN1 patients remained consistent over the study period (range, 24-31%).

Multivariable risk difference regression: Predictors of undergoing initial RP for cN1 PCa Patients

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>pN1 (N=3079)</th>
<th>cN1 (N=11,249)</th>
<th>Hazard Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White race</td>
<td>0.74 (0.68-0.80)</td>
<td>1.00 (1.00-1.00)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Charlson score ≥ 0</td>
<td>1.38 (1.27-1.50)</td>
<td>1.00 (1.00-1.00)</td>
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<td></td>
</tr>
<tr>
<td>Private Insurance</td>
<td>0.47 (0.42-0.52)</td>
<td>0.48 (0.43-0.53)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Age &gt; 65</td>
<td>0.60 (0.55-0.65)</td>
<td>0.70 (0.65-0.74)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>PSA ≥ 20</td>
<td>0.72 (0.66-0.78)</td>
<td>0.67 (0.62-0.72)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Gleason score ≥ 8</td>
<td>0.59 (0.54-0.65)</td>
<td>0.79 (0.74-0.85)</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

 Baseline Characteristics

- Age at diagnosis, median (IQR): 66 (60,73) for white race; 8.936 (80.6%) with Charlson score ≥ 0.
- Gleason score ≥ 8; 7,156 (73.2%); PSA ≥ 20; 5,162 (49.9%); T stage ≥ 2c: 6,342 (59.2%)

Survival in pN1 patients by initial clinical node status

<table>
<thead>
<tr>
<th>Hazard Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White race</td>
<td>1.00 (0.86-1.16)</td>
</tr>
<tr>
<td>Charlson score ≥ 0</td>
<td>1.28 (1.10-1.49)</td>
</tr>
<tr>
<td>Private Insurance</td>
<td>0.57 (0.50-0.66)</td>
</tr>
<tr>
<td>Age &gt; 65</td>
<td>1.27 (1.13-1.43)</td>
</tr>
<tr>
<td>PSA ≥ 20</td>
<td>1.31 (1.17-1.47)</td>
</tr>
<tr>
<td>Gleason score ≥ 8</td>
<td>1.90 (1.70-2.12)</td>
</tr>
</tbody>
</table>

CONCLUSIONS

• The initial treatment of regional risk cN1 disease is highly variable, with approximately 1 in 4 patients undergoing RP from 2004-2016.
• Factors associated with higher likelihood of RP include younger age, white race, private insurance, and lower Gleason score and PSA.
• The majority of cN1 patients who undergo RP are confirmed pN1, and most of these patients undergo post-operative RT and/or ADT.
• Among patients with pN1 disease on RP, clinical nodal staging retains prognostic significance for OS.
• These findings underscore the utility of initial clinical staging when considering initial and adjuvant treatments for regional risk patients.

LIMITATIONS

• For the pN1 cohort, although clinical node positive remained significantly associated with worse OS on multivariable analysis, other patient- and disease-specific factors (age, comorbidity, disease stage and Gleason score, type of treatment site, and insurance status) were stronger predictors of survival.
• Of cN1 patients who underwent prostatectomy, pathologic staging information was unavailable for 29% of patients (N=888).
• Over 80% of patients had a coded Charlson score of 0; this likely did not fully capture the comorbidity profiles of this elderly population, and may reflect an ascertainment bias resulting in a counterintuitive link between higher Charlson score and higher likelihood of RP.

ACKNOWLEDGEMENTS

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