# 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 many 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).

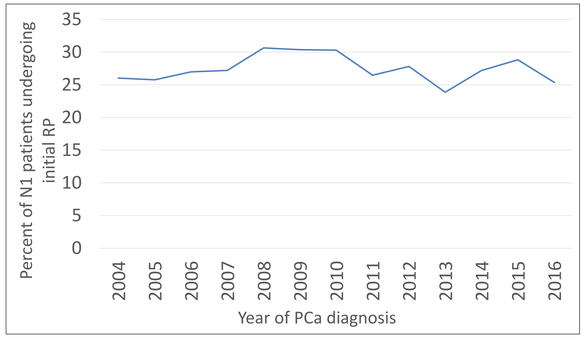
### Baseline Characteristics

| cN1 Cohort (N=11,249) | N (%) |
|---|---|
| Age at diagnosis, median (IQR) | 66 (60, 73) |
| White race | 8,936 (80.6%) |
| Charlson score > 0 | 2,073 (18.4%) |
| Gleason score ≥ 8 | 7,156 (73.2%) |
| PSA ≥ 20 | 5,162 (49.9%) |
| T stage ≥ 2c | 6,342 (59.2%) |

| pN1 Cohort (N=17,909) | N (%) |
|---|---|
| Age at diagnosis, median (IQR) | 63 (57, 67) |
| White race | 14,878 (84.3%) |
| Charlson score > 0 | 3,430 (19.2%) |
| Gleason score ≥ 8 | 9,741 (56.7%) |
| PSA ≥ 20 | 4,022 (24.5%) |
| T stage ≥ 2c | 4,270 (28.3%) |

## RESULTS

### Annual Rates of RP in cN1 PCa Patients



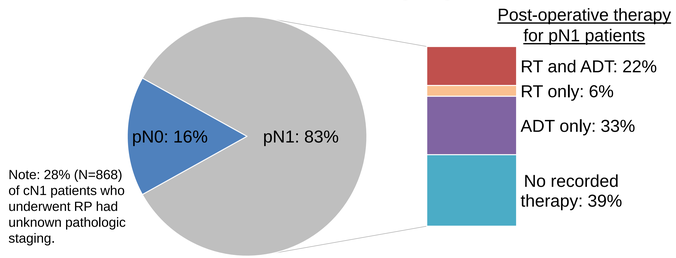

- Overall, 27% (N=3079) of patients with cN1 disease underwent initial RP.
- Annual rates of initial RP for cN1 patients remained consistent over the study period (range, 24-31%).

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

| | Incidence Risk ratio (95% CI) | P value |
|---|---|---|
| White race | **1.33 (1.20-1.47)** | **<0.001** |
| Age>65 | **0.74 (0.68-0.80)** | **<0.001** |
| Treatment at academic center | **1.08 (1.01-1.15)** | **0.026** |
| Private insurance | **1.24 (1.14-1.35)** | **<0.001** |
| Top half median income | 0.98 (0.91-1.05) | 0.624 |
| Charlson score > 0 | **1.21 (1.11-1.31)** | **<0.001** |
| T stage ≥ 2c | **1.18 (1.10-1.26)** | **<0.001** |
| PSA ≥ 20 | **0.67 (0.63-0.72)** | **<0.001** |
| Gleason ≥ 8 | **0.79 (0.74-0.85)** | **<0.001** |

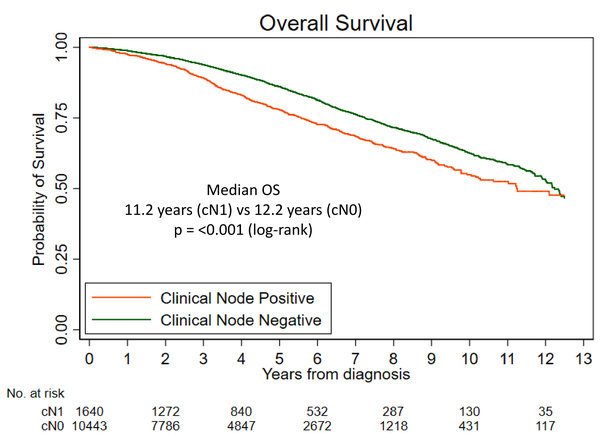
- White race, age ≤ 65, treatment at an academic center, private insurance, CCI > 0, T stage ≥ 2c, PSA ≤ 20, and Gleason score < 8 were associated with higher likelihood of initial RP for cN1 patients.

### Post-Surgical Staging and Treatment for cN1 PCa Patients Undergoing Initial RP




- Of cN1 patients who underwent RP and had pathologic staging available (n=2,211), 84% (n=1,851) were confirmed pN1 and 16% (n=360) were pN0.
- 61% of cN1 patients who were pN1 on prostatectomy (N=1,126) underwent post-operative RT and/or ADT.

### Survival in pN1 patients by initial clinical node status




- Among 14,365 PCa patients with pN1 disease after RP:
  - 13% (N=1,841) were initially staged as cN1
  - 87% (N=12,514) were initially staged as cN0
- cN1 patients had worse survival compared to cN0 patients (mOS 11.2 years vs. 12.2 years, p<0.001 on log-rank test).
- 5-year overall survival was 86% for cN0 patients and 78% for cN1 patients.

### Multivariable Cox survival analysis: Factors associated with overall survival in pN1 patients

| | Hazard Ratio (95% CI) | P value |
|---|---|---|
| Clinical N1 | **1.15 (1.00-1.32)** | **0.049** |
| White race | 1.00 (0.86-1.16) | 0.989 |
| Age>65 | **1.26 (1.10-1.43)** | **0.001** |
| Treatment at academic center | **0.77 (0.70-0.86)** | **<0.001** |
| Private insurance | **0.86 (0.75-0.97)** | **0.019** |
| Top half median income | 0.90 (0.81-1.00) | 0.041 |
| Charlson score > 0 | **1.27 (1.13-1.43)** | **<0.001** |
| T stage ≥ 2c | **1.31 (1.17-1.47)** | **<0.001** |
| PSA ≥ 20 | 1.03 (0.92-1.16) | 0.576 |
| Gleason ≥ 8 | **1.90 (1.70-2.12)** | **<0.001** |

- After adjustment for practice setting, patient, and disease variables, initial cN1 clinical stage remained significantly associated with worse overall survival **(HR = 1.15, p=0.049).**
- However, other factors were more strongly associated with survival, and accounted for much of the unadjusted difference in survival between cN0 and cN1 groups.
  - Age > 65, treatment at a non-academic center, non-private insurance, lower median income, Charlson score > 0, T stage ≥ 2c, and GS ≥ 8 were associated with worse overall survival.

## 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 positivity 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 28% of patients (N=868).
- 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.

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