

# Low Use of Immediate and Delayed Postoperative Radiation for Prostate Cancer with Adverse Pathological Features

Matthew J. Maurice, Hui Zhu and Robert Abouassaly\*

From the Urology Institute, University Hospitals Case Medical Center (MJM, RA), Louis Stokes Cleveland Veterans Affairs Medical Center (MJM, HZ) and Glickman Urologic and Kidney Institute, Cleveland Clinic (HZ), Cleveland, Ohio

## Abbreviations and Acronyms

APF = adverse pathological features  
CCI = Charlson comorbidity index  
dRT = delayed radiotherapy  
iRT = immediate radiotherapy  
NCDB = National Cancer Data Base  
PC = prostate cancer  
PSA = prostate specific antigen  
PSM = positive surgical margin  
RCT = randomized controlled trial  
RP = radical prostatectomy  
RT = radiotherapy

Accepted for publication March 27, 2015.  
Study received institutional review board approval.

The American College of Surgeons and Commission on Cancer have not verified and are not responsible for the analytical or statistical methodology employed or the conclusions drawn from these data by the investigator.

\* Correspondence: Urology Institute, University Hospitals Case Medical Center, 11100 Euclid Ave., Mailstop LKS 5046, Office 4565, Cleveland, Ohio 44106 (telephone: 216-844-4831; FAX: 216-844-7735; e-mail: [robert.abouassaly@uhhospitals.org](mailto:robert.abouassaly@uhhospitals.org)).

Presented at annual meeting of American Urological Association, Orlando, Florida, May 20, 2014.

**Purpose:** Level 1 evidence supports immediate radiation in post-prostatectomy patients with adverse pathological features while analogous evidence for delayed radiation is lacking. We evaluated immediate and delayed radiation practice patterns and identified factors affecting their use.

**Materials and Methods:** Using the National Cancer Data Base we identified 57,448 men diagnosed with pT3 disease and/or positive margins from 2004 to 2009. Postoperative radiation use through 2011 was analyzed by time trends and multivariate analysis.

**Results:** A total of 4,316 men (7.5%) received immediate radiation, 1,637 (2.8%) received delayed radiation and 51,495 (90%) were observed. Immediate and delayed radiation use remained relatively stable except for a small but significant decrease in immediate radiation in 2008. This decrease was associated with a relative increase in delayed radiotherapy. Compared to 2004 men diagnosed in 2007 to 2009 had 1.3-fold to 1.5-fold higher odds of delayed radiation than of immediate radiation ( $p < 0.01$ ). The strongest predictors of immediate radiation were margin status, T stage, N stage, Gleason score and patient age. Men with positive margins, seminal vesicle invasion, nodal disease, or Gleason score 8 or greater and younger men had 2.3-fold to sixfold greater odds of receiving immediate radiation than observation ( $p < 0.01$ ). Men with positive margins, seminal vesicle invasion or nodal metastases were also more likely to receive immediate rather than delayed radiation ( $p < 0.01$ ).

**Conclusions:** Post-prostatectomy radiation is performed sparingly. Immediate radiation rates remain low but do not appear to be influenced substantially by delayed radiation use. Consistent with the evidence, patients at high risk for recurrence are more likely to undergo immediate radiation rather than observation or delayed radiation.

**Key Words:** prostatic neoplasms; prostatectomy; radiotherapy, adjuvant; salvage therapy; neoplasm recurrence, local

Up to 40% of men with PC experience biochemical recurrence following RP.<sup>1</sup> Men with APF, such as extraprostatic extension, PSM or seminal vesicle invasion, are at highest risk for post-RP recurrence.<sup>2,3</sup> Since 2005, 3 RCTs have shown that iRT improves oncologic outcomes in these men.<sup>4-6</sup> However, many men with these risk

factors do not experience progression and, thus, they are overtreated with iRT and exposed unnecessarily to its toxicity.<sup>7-10</sup> Alternatively dRT, which is supported only by retrospective data, may offer oncologic outcomes comparable to those of iRT while potentially minimizing overtreatment and its associated harms.<sup>11,12</sup>

Consequently there is significant controversy regarding the appropriate timing and triggers of post-RP RT in the treatment of patients with APF.

Historically iRT use has been low.<sup>13</sup> While several studies have shown that contemporary application of iRT has remained low despite supporting level 1 evidence, the impact of dRT use on this trend has not been elucidated.<sup>14–16</sup> We hypothesized that increased dRT may be supplanting iRT. To answer this question we evaluated iRT and dRT use, and identified factors predicting use.

## MATERIALS AND METHODS

### Data Source

The NCDB, a joint project of the American Cancer Society® and the American College of Surgeons Commission on Cancer, is a comprehensive clinical oncology database that captures 70% of all incident malignancies in the United States. We used the NCDB participant user file, which encompasses diagnosis years 1998 to 2011. Since the data set is completely de-identified, our study qualified for institutional review board exemption.

### Study Population

We identified 764,088 patients diagnosed with PC between 2004 and 2009 based on ICD-O-3 primary site coding (C619). Diagnoses prior to 2004 were excluded from study because Gleason scores were unavailable. Diagnoses after 2009 were omitted to permit at least 2 years of followup data for each diagnosis year. We restricted our cohort to 58,703 patients with no prior history of malignancy who had pT3 disease and/or PSM after RP. The 466 cases diagnosed but not treated at the reporting facility were excluded from analysis because of missing followup data. We excluded 743 patients who received neoadjuvant or intraoperative radiation therapy, given unclear indications. Finally, 46 cases in which radiation was administered greater than 2 years after RP were excluded to avoid censoring. In the final cohort 57,448 patients were available for analysis.

### Study Variables

We evaluated the relationship of temporal, demographic, clinical and provider factors with post-RP RT use. Demographic factors included area of residence, education level, income level and insurance type. Area of residence was defined as urban, metropolitan or rural based on data from the 2003 United States Department of Agriculture Research Service. Education and household income levels were estimates based on 2000 United States Census data. Education level, defined by the high school dropout rate, was categorized as highest—less than 14%, upper middle—14% to 19.9%, lower middle—20% to 28.9% and lowest—29% or greater. Income level, defined by annual income quartiles, was categorized as lowest—less than \$30,000, lower middle—\$30,000 to \$35,000, upper middle—\$35,000 to \$46,000 and highest—greater than \$46,000. Insurance was grouped as uninsured, private/managed care and federal/social (Medicare/Medicaid). Clinical factors included race, age at diagnosis, CCI, Gleason score (6 or less, 7 and 8 or greater),

pathological T stage (pT2 and pT3), pathological N stage (pN0, pN1 and pNx) and surgical margin status (R0 and R1). Race was categorized as nonHispanic Caucasian, African-American, Hispanic or other. Age was grouped by decades. CCI was calculated based on ICD-9-CM secondary diagnosis codes and categorized as 0 (no comorbid conditions), 1 or greater than 1.

Provider factors included hospital type, hospital PC volume and geographic location. Hospital type is designated by the CoC and includes academic, comprehensive, community and other cancer programs.<sup>17</sup> Hospital volume was calculated based on the overall number of PC cases with APF treated per hospital. Hospitals were then categorized into tertiles by overall volume. Location was divided into regions based on the state of the reporting facility, including Northeast, Midwest, South and West.

### Endpoints

The primary endpoints of our study were iRT and dRT use among post-RP patients with APF between 2004 and 2009. Post-RP RT was defined as external beam or other radiation to the prostate and/or pelvis initiated within 2 years of RP. RT was classified as iRT if initiated within 4.5 months of surgery based on the strict RCT definition or as dRT if occurring later. Since the RCTs defined adjuvant RT as RT within 3 to 4 months of RP, 20% to 33% of included men had detectable PSA.<sup>4–6</sup>

### Statistical Analyses

Annual iRT and dRT use rates were calculated by dividing the number of patients treated in each interval by the total number of yearly diagnoses. Univariate analysis was performed by the Pearson chi-square test. Multivariate logistic regression was performed with iRT (vs observation) as the response variable and with diagnosis year and the other study variables as covariates (supplementary table 1, <http://jurology.com/>). Analysis was rerun using iRT (vs dRT) as the response variable and the same covariates. Statistical tests were performed with SAS®, version 9.1 with  $p < 0.05$  considered statistically significant.

## RESULTS

The study cohort was composed predominantly of healthy, middle-aged or older, high school educated, middle class, insured white men living in metropolitan areas who sought care at major academic and comprehensive community cancer centers throughout the United States (supplementary table 1, <http://jurology.com/>). Most men had Gleason 7-10 pT3aN0R0/1 disease.

Overall from 2004 to 2009, 10% of these men (5,953 of 57,448) underwent post-RP RT while the remaining 51,495 were observed. In the treatment group 7.5% of men (4,316 of 57,448) received iRT and 2.8% (1,637 of 57,448) received dRT.

During the study period iRT use remained stable (range 6.5% to 8.4%) except for a small but significant decrease in 2008 (supplementary table 2, <http://jurology.com/>, see figure). Similarly dRT use was static overall (range 2.5% to 3.2%). However,

Download English Version:

<https://daneshyari.com/en/article/3859984>

Download Persian Version:

<https://daneshyari.com/article/3859984>

[Daneshyari.com](https://daneshyari.com)