Original Study

What Is the Optimal Management of Gleason Score 7 Prostate Cancer at Biopsy? A Comparison of Disease Control for Prostatectomy Versus Radiotherapy

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Abstract

Gleason 7 prostate cancer remains a challenging clinical entity, and either prostatectomy or radiotherapy may be used. We sought to compare outcomes of these approaches within our community experience, including 207 eligible patients treated over an 8-year period, with mature follow-up. The 5-year prostate-specific antigen control was superior for radiotherapy; however, no difference in prostate cancer–specific survival was evident.

Objectives: To compare outcomes between radical prostatectomy (RP) or radiotherapy (RT) approaches for Gleason 7 (GS7) prostate cancer. **Methods:** Patients were retrospectively identified for inclusion by clinically localized disease, GS7, prostate-specific antigen (PSA) < 30 ng/mL at diagnosis, and follow-up with PSA at > 12 months. Comparison of demographic, tumor, staging, and outcome variables was performed. Disease recurrence was defined as per contemporary society guidelines. The Kaplan-Meier method was used for disease control estimates. **Results:** Between 2003 and 2010, a total of 253 patients were diagnosed with GS7 prostate cancer, of whom 207 were eligible for the current analysis (120 RP, 87 RT). Excepting older age for RT patients (median 73 vs. 62 years), the groups were well balanced. For RP patients, 82 patients (60%) had at least 1 high-risk feature, 4 (5%) of whom received adjuvant RT. For RT patients, 71 patients (82%) received hormone therapy (median duration 6 months). At a median follow-up of 62.2 months (range 13.1-136.6 months, with no difference between treatment groups), 64 patients had PSA relapse (51 RP, 13 RT), and 15 had died (5 of or with disease). PSA relapse-free survival was inferior for RP versus RT ($P < .0001$), with 5-year rates of 55.4% versus 82.6%, respectively. **Conclusion:** For GS7 prostate cancer patients, RT is associated with superior disease-free survival at 5 years compared to RP alone, without difference in disease-specific survival. Whether this difference remains in the setting of appropriately used adjuvant RT after RP, and the effect of possible delay in testosterone recovery for older RT patients remain to be determined.

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Introduction

Patients diagnosed with clinically localized Gleason 7 (GS7) prostate cancer are characterized by heterogeneity, both in terms of management recommendations and disease control outcomes.[1] At present, patients without significant medical comorbidities may consider either surgical or nonsurgical approaches with curative intent.[2] For patients undergoing radical prostatectomy (RP), high-risk pathologic features such as extraprostatic extension, involved surgical margins, and/or seminal vesicle invasion are often identified,[3,4] for which postoperative radiotherapy (RT) is presently recommended, based on the results of several large multicenter phase III trials.[5-7] Alternatively, patients treated with RT up front are recommended to receive short-course (4 to 6 months) testosterone suppression hormone therapy (HT).[2,8,9] At present, there are no randomized trials and few quality studies comparing the outcomes of these approaches specific to GS7 prostate cancer. The present investigation reports on disease control and survival outcomes for this population.

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Materials and Methods

After receipt of institutional review board approval at the study institutions, a research database was created with study-specific patient, treatment, and outcome data fields. Eligible cases were identified by review of medical records and a quality assurance database. After selection for prostate adenocarcinoma cases, a review of patient records was performed in order to eliminate patients with advanced or metastatic disease at diagnosis (including pretreatment evidence of seminal vesicle or pelvic lymph node involvement), prostate-specific antigen (PSA) of $\geq$ 30 ng/mL (owing to high risk of occult micrometastatic disease), or Gleason score $\leq$ 6 or $\geq$ 8 at biopsy. Owing to standard recommendation for HT use for the RT group,[2] a minimum follow-up of 12 months after treatment was required (unless there was prior recurrence or death) and applied to both groups for uniformity.

For the RP group, decision to refer or treat with immediate postoperative (adjuvant) therapy was left to the discretion of the managing urologist. For the RT group, decision to use external-beam RT, brachytherapy, or both was left to the discretion of the treating radiation oncologist. For definitive external-beam RT, doses of 70 to 79.2 Gy in standard fractionation (1.8 to 2 Gy per once-daily fraction, 5 days per week) were used, with all but 6 receiving $\geq$ 75.6 Gy. For patients treated with brachytherapy alone, ^{103}Pd unstranded seeds were implanted, with intraoperative planning and minimum target (prostate) D90 of 125 Gy. For patients treated with a combined approach, implants with a minimum target D90 of 90 to 100 Gy were, followed 8 to 10 weeks later by 45 to 50.4 Gy external-beam RT to the prostate and seminal vesicles (standard fractionation). Decision to use HT was left to the discretion of the treating radiation oncologist–urologist team, taking into account patient decision and comorbidities. When used, HT involved gonadotropin-releasing hormone agonist alone, initiated 8 to 12 weeks before the first RT intervention.

Posttreatment evaluations included physical examination and PSA measurement every 3 to 6 months for the first 2 years after treatment, and every 6 to 12 months thereafter. In the setting of PSA or clinical relapse, restaging imaging and subsequent interventions were performed at the discretion of the managing physicians.

The principal outcome measure of this retrospective study was freedom from failure, measured from date of RP or RT initiation. Events for freedom from failure included either PSA relapse or clinical or radiographic evidence of disease recurrence. Contemporary definitions of PSA relapse were used, including PSA of 0.2 ng/mL and rising for the RP group,[2] and nadir plus 2 ng/dL for the RT group,[9] or at initiation of salvage therapy for either group.

Kaplan-Meier survival curves were constructed to describe freedom from failure and overall survival for the entire cohort. The Cox proportional hazards model was used to identify continuous and dichotomous variable association with disease control; categorical variables were analyzed by log-rank analysis. Analyses were performed by SPSS software, version 21 (IBM, Armonk, NY, USA).

Results

Between 2003 and 2010, a total of 253 patients were diagnosed with GS7 prostate cancer at the treating institutions. Of these, 207 were eligible for the current analysis, including 120 RP and 87 RT. Reasons for exclusion were PSA $\geq$ 30 ng/mL (6 RP patients, 8 RT), insufficient follow-up (9 RP, 12 RT), clinically advanced or node-positive disease (2 RT), and other factor (3 RP, 6 RT). Patient demographics and pretreatment tumor characteristics are displayed in Table 1. Excepting older age for RT patients (median age 73 vs. 62 years; $P < .0001$) and nonsignificant difference in primary Gleason grade (higher grade for RT; 41% vs. 30%; $P = .091$), the treatment groups were well balanced.

Pathology and treatment specifics for the RP group are listed in Table 2. All patients underwent retroperitoneal approach (6 robot-assisted laparoscopic technique), and 103 (86%) were nerve sparing. Median prostate volume at pathology was 42.7 cm^3 (range 20-240 cm^3). In terms of pathologic features, 82 (60%) had at least 1 high-risk feature (including 59 patients with involved margins and 16 patients with seminal vesicle involvement), 4 (5%) of whom received adjuvant RT (within 4 months, before PSA relapse).

For the RT group, external-beam RT alone was provided to 42 patients (48%), brachytherapy to 36 (41%), and a combination to 9 (10%). The median definitive external-beam dose completed was 75.6 Gy (range 70-79.2 Gy), and for the brachytherapy-alone

Table 1 Patient Demographics, Tumor Characteristics, and Staging Evaluations

Characteristic	RP (n = 120)	RT (n = 87)	*P*
Age (years)			<.0001
Median	62	73	
Range	44-74	50-83	
≥65 years	45 (35%)	68 (78%)	
Race			NS
White	119 (99%)	85 (98%)	
PSA (ng/mL)			.124
Median	5.9	7.2	
Range	1.8-29.3	2.4-27.1	
20 ng/mL	10 (8%)	4 (5%)	
Gleason Score			.091
3+4	84 (70%)	51 (59%)	
4+3	36 (30%)	36 (41%)	
cT Stage[a]			NS
cT1b	0	3 (3%)	
T1c	89 (74%)	54 (62%)	
T2a	19 (16%)	22 (25%)	
T2b	5 (4%)	7 (8%)	
T2c	4 (3%)	0	
T3a	1 (1%)	1 (1%)	
Cores Involved (%)			NS
Median	38.8	41.4	
Range	5-75	6-83	
Staging Studies			NS
CT	8 (7%)	9 (10%)	
Bone scan	47 (39%)	35 (40%)	

Abbreviations: PSA = prostate-specific antigen; RP = radical prostatectomy; RT = radiotherapy.
[a]American Joint Committee on Cancer, tumor, node, metastasis classification system, version 7.0.