Trifecta Outcomes for Men with Localized Prostate Cancer after Treatment with Low-Dose-Rate Brachytherapy

Marissa Kent, MD, Jared Winoker, MD, Richard Stock, MD, Nelson Stone, MD

ABSTRACT:

Introduction: The ideal outcomes in prostate cancer (PCa) treatment have been described as a ″trifecta″. This term denotes the desired triad of oncologic control, urinary continence, and sexual potency. We sought to determine the probability of achieving these results and the risk factors associated with trifecta failure in men treated with brachytherapy (BT) for localized PCa.

Methods: From 1990 to 2011, 734 men meeting trifecta criteria at baseline were treated with low-dose-rate BT with or without external beam radiation therapy (EBRT) and underwent ≥5 years of follow-up. Included men had clinical stage T1-T2 PCa, International Prostate Symptoms Score (IPSS) ≤ 7, and good erectile function (EF), defined as Sexual Health Inventory for Men (SHIM) score >17 or Mount Sinai Erectile Function (MSEF) score 2-3. Post-treatment trifecta failure was defined as biochemical recurrence (BCR) by Phoenix criteria (prostate specific antigen (PSA) nadir +2 ng/ml), increase in IPSS ≥5, or EF decline (SHIM <17 or MSEF 0-1). Patients with baseline incontinence or missing data were excluded. Univariate associations were calculated with chi-square and ANOVA. Logistic regression analysis was used to identify factors predictive of trifecta failure at 2 and 5 years post-treatment.

Results: Median follow up was 10 years (range 5-22). Mean age at treatment was 64 years (range 41-83). 66% (297/451) failed to achieve trifecta criteria at 2 years and 68% (250/366) at 5 years. Worsened urinary function was the most common reason for trifecta failure at 2 years (48%) but accounted for just 28% of failure at 5 years. EF decline was the main reason for failure at 5-year (58%) follow-up. Phoenix failure was uncommon (≤2%). On multivariate analysis, age >65 was prognostic for 5-year failure, but not at 2-year. No other clinical or treatment related factors were significant.

Conclusions: Trifecta outcomes were attained in 34% and 32% of patients at 2 and 5-year follow-up with ED accounting for the majority of trifecta failure at 5-year follow up. Cancer control was excellent and treatment related urinary symptoms improved over time, trending back toward baseline with longer follow-up. Age >65 was predictive of long-term trifecta failure. Further work is needed to better risk stratify patients before BT to expect functional outcomes and improve individualization of care.

INTRODUCTION:

Radiation therapy is a well established treatment for prostate cancer.1 When discussing the ideal outcome of prostate cancer treatment, many urologists have started using the concept of "trifecta"outcomes. In the context of prostate surgery, this "trifecta" refers to cancer control, urinary continence and sexual potency.2-3

Although this criteria for success has caught on among urologists performing radical prostatectomies, it has not gained as much popularity in the literature among radiation oncologists performing radiotherapy. Given the fact that many patients are often left to chose between radiotherapy and surgery, it would be helpful to have the same "trifecta" criteria rates for those who undergo radiotherapy.

The objective of this study is to determine the probability of achieving trifecta results if one undergoes radiation therapy and to determine the risk factors associated with trifecta failure in men treated with brachytherapy for localized PCa.

METHODS :

From 1990 to 2011, 734 men meeting trifecta criteria at baseline were treated with low-dose-rate BT with or without external beam radiation therapy (EBRT) and underwent ≥5 years of follow-up.

Included men had clinical stage T1-T2 PCa, International Prostate Symptoms Score (IPSS) ≤ 7, and good erectile function (EF), defined as Sexual Health Inventory for Men (SHIM) score >17 or Mount Sinai Erectile Function (MSEF) score 2-3. Post-treatment trifecta failure was defined as biochemical recurrence (BCR) by Phoenix criteria (prostate specific antigen (PSA) nadir +2 ng/ml), increase in IPSS ≥5, or EF decline (SHIM <17 or MSEF 0-1). Patients with baseline incontinence or missing data were excluded.

Univariate associations were calculated with chi-square and ANOVA. Logistic regression analysis was used to identify factors predictive of trifecta failure at 2 and 5 years post-treatment.

RESULTS:

Seven-hundred and thirty-four men met inclusion criteria. Median follow up was 10 years (range 5-22). Mean age at treatment was 64 years (range 41-83).

Sixty-six percent (297/451) failed to achieve trifecta criteria at 2 years and 68% (250/366) at 5 years. Worsened urinary function was the most common reason for trifecta failure at 2 years (48%) but accounted for just 28% of failure at 5 years. EF decline was the main reason for failure at 5-year (58%) follow-up. Phoenix failure was uncommon (≤2%).

On multivariate analysis, age >65 was prognostic for 5-year failure, but not at 2-year. No other clinical or treatment related factors were significant.

Predictors of Trifecta failure at 2- and 5-year follow-up

Variables	2-YEARS					5-YEARS				
	Univariate			Multivariate		Univariate			Multivariate	
	n	Failure (%)	p	OR	p	n	Failure (%)	p	OR	p
Race			0.043					0.914		
Caucasian	360	246 (68%)		-1.27	0.238	286	195 (68%)		0.103	0.909
African American	55	28 (51%)		-1.93	0.08	44	29 (66%)		0.009	0.993
Hispanic	25	14 (56%)		-1.8	0.114	25	19 (43%)		0.326	0.747
Asian	2	1 (50%)		-2.13	0.232	5	3 (60%)		-0.143	0.912
Age >65 years	198	131 (66%)	0.903	0.054	0.799	170	130 (76%)	0.002	0.64	0.008
PSA =10 ng/ml	91	53 (58%)	0.087	-0.18	0.579	81	60 (74%)	0.206	-0.201	0.622
BED =200 Gy₂	244	163 (67%)	0.644	0.227	0.232	189	131 (69%)	0.669	0.148	0.543
EBRT	160	102 (64%)	0.485	-0.16	0.643	120	89 (74%)	0.092	-0.84	0.832
HT	189	117 (62%)	0.133	-0.05	0.85	156	116 (74%)	0.032	0.222	0.464
NCCN RG			0.415					0.004		
Low	232	158 (68%)				189	115 (61%)			
Intermediate	101	67 (66%)		0.13	0.822	90	72 (80%)		-0.355	0.613
High	118	72 (61%)		0.176	0.652	87	63 (72%)		0.497	0.31
Stage			0.878	0.191	0.594			0.07	0.169	0.705
T1	330	218 (66%)				278	183 (66%)			
T2	121	79 (65%)				88	67 (76%)			

Key: BED=biological effective dose, EBRT=external beam radiation therapy, HT=hormone therapy, NCCN RG=NCCN Risk Group Classification

CONCLUSIONS:

Trifecta outcomes were attained in 34% and 32% of patients at 2 and 5-year follow-up with ED accounting for the majority of trifecta failure at 5-year follow up.

Cancer control was excellent and treatment related urinary symptoms improved over time, trending back toward baseline with longer follow-up.

Age >65 was predictive of long-term trifecta failure.

Further work is needed to better risk stratify patients before BT to expect functional outcomes and improve individualization of care.

REFERENCES:

1. Jereczek-Fossa BA, Orecchia R. Evidence-based radiation oncology: definitive, adjuvant and salvage radiotherapy for non-metastatic prostate cancer. Radiother Oncol 2007; 84: 197–215
2. Bianco FJ Jr, Scardino PT, Eastham JA. Radical prostatectomy: long-term cancer control and recovery of sexual and urinary function ('trifecta'). Urology 2005; 66 (Suppl.): 83–94
3. Ficarra V, Sooriakumaran P, Novara G et al. Systematic review of methods for reporting combined outcomes after radical prostatectomy and proposal of a novel system: the survival, continence, and potency (SCP) classification. Eur Urol 2012; 61: 541–8
4. Arcangeli S, Strigari L, Gomellini S et al. Updated results and patterns of failure in a randomized hypofractionation trial for high-risk prostate cancer. *Int J Radiat Oncol Biol Phys* 2012; 84: 1172–8