Managing Cancer Relapse After Radical Prostatectomy

Adjuvant Versus Salvage Radiation Therapy

Joseph F. Rodriguez, MD[a,*], Stanley L. Liauw, MD[b], Scott E. Eggener, MD[a]

KEYWORDS

• Prostate • Cancer • Adjuvant • Salvage • Radiotherapy

KEY POINTS

- Disease recurrence following radical prostatectomy is common in men with extraprostatic extension and seminal vesicle invasion with or without positive margins.
- Postoperative adjuvant radiation therapy reduces the risk of risk of biochemical recurrence by approximately half and may improve overall survival.
- Retrospective studies suggest similar efficacy of salvage radiotherapy administered at the time of detectable prostate-specific antigen.
- Patient selection for postoperative radiotherapy is a challenge and current focus of research.

INTRODUCTION

Approximately 1 in 6 men in the United States is diagnosed with prostate cancer.[1] Only 10% to 15% of these men eventually die from their disease, yet more than 25,000 deaths per year are attributed to prostate cancer in the United States.[2] Because of this disparity, identifying those with aggressive disease for early curative therapy while limiting the overtreatment of indolent disease is paramount. Radical prostatectomy (RP) can be curative for men with localized prostate cancer.[3] However, following RP, approximately 30% of men experience biochemical recurrence (BCR), the redetection of prostate-specific antigen (PSA) in the blood, within 10 years.[4–6] The aim of this article was to discuss adjuvant and salvage radiation therapy following RP.

PREDICTING RELAPSE AFTER RADICAL PROSTATECTOMY

Preoperative PSA, pathologic tumor stage (pT), Gleason grade, and margin status have been used to estimate rates of BCR following RP. BCR after RP is most often defined as PSA $\geq$0.2 ng/mL when previously undetectable, although more than 50 definitions have been published.[7] **Table 1** outlines data from more than 10,000 men treated by RP and their associated rates of BCR stratified by risk factors. At 10 years, most men experience BCR with pT3 disease (extraprostatic extension [EPE]; or seminal vesical invasion [SVI]), with or without positive surgical margins (+SMs). For organ-confined cancers, +SMs are associated with a risk of BCR of 30% to 40%, increasing to greater than 50% when associated with

Disclosures: None.

[a] Section of Urology, University of Chicago, The University of Chicago Medicine, 5841 South Maryland Avenue, MC 6038, Chicago, IL 60637, USA; [b] Department of Radiation and Cellular Oncology, University of Chicago, The University of Chicago Medicine, 5758 South Maryland Avenue, MC 9006, Chicago, IL 60637, USA
* Corresponding author.
E-mail address: tony.rodriguez17@gmail.com

Urol Clin N Am 44 (2017) 597–609
http://dx.doi.org/10.1016/j.ucl.2017.07.011

Table 1
Percentages of patients with biochemical recurrence at 10 years post-prostatectomy stratified by risk factors

Study	Overview	Risk Factors	%BCR-10 y
8 Centers	1983–2000	+SM	64
Karakiewicz	25 mo med f/u	EPE +SM/−SM	75/54
Urol 2005	39% BCR overall	SVI +SM/−SM	88/80
n = 5831	0% adjuvant	LNI +SM/−SM	92/86
Washington University	1983–2003	Gleason ≥8	68
Roehl	65 mo med f/u	EPE +SM/−SM	47/38
J Urol 2004	32% BCR overall	SVI	74
n = 3478	6% adjuvant	LNI	88
Baylor	1983–1998	+SM	64
Hull	47 mo med f/u	EPE alone	29
J Urol 2002	25% BCR overall	SVI	63
n = 1000	0% adjuvant	LNI	93

Abbreviations: +SM, positive surgical margin; −SM, negative surgical margin; BCR, biochemical recurrence; EPE, extraprostatic extension; f/u, follow-up; LNI, lymph node invasion; med, median; SVI, seminal vesical invasion.

Gleason ≥7 disease.[8] Another strong predictor of BCR, lymph node invasion, has been associated with greater than 85% risk of BCR.[4,6,9]

Nomograms have been developed using these post-RP variables to individualize a patient's risk of disease recurrence. The Stephenson nomogram was modeled from more than 2000 patients treated from 1983 to 2003 at 5 US academic centers.[10] A 10-year progression-free (BCR-free) probability can be predicted from pretreatment PSA, year of RP, SM status, pathologic stage, lymph node status, Gleason score, and time from surgery. An electronic version can be accessed at https://www.mskcc.org/nomograms/prostate/post-op.

The CAPRA-S scoring system was developed from the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) national disease registry which includes over 3800 patients.[11] It uses many of the same variables as the Stephenson nomogram to assign patients to 1 of 10 risk categories for recurrence at 3 and 5 years following RP (**Table 2**). Both of these tools have been externally validated and can help personalize prognosis and improve decision making.[12,13]

INCREASING UTILIZATION OF RADICAL PROSTATECTOMY FOR LOCALLY ADVANCED DISEASE

Nomograms like Stephenson and CAPRA-S are particularly useful, as the proportion of patients having RP with adverse pathologic features is increasing.[14] Most men choose RP for the initial treatment of localized prostate cancer over other modalities, and that proportion has been increasing since the early 2000s.[15]

Part of this increase in RP may be attributed to decreased utilization of primary hormonal therapy, which at the cost of significant morbidity does not improve overall survival and is not recommended for localized disease.[16] The rise of active surveillance as a management strategy for men with low-risk disease contributes to a higher proportion of men undergoing RP with more advanced disease. Additionally, surgery over radiation for the management of clinically localized, high-risk prostate cancer has been increasing.[17]

Changes in prostate cancer screening may also contribute to the numbers of patients with locally advanced disease undergoing RP. In 2008, the United States Preventative Services Task Force (USPSTF) recommended against PSA screening for patients 75 years and older.[18] This was followed in 2012 by a recommendation discouraging PSA screening for all men.[19] Statistical modeling by Shen and Kumar[20] estimates the "trade-off effect" of PSA screening is 1 less patient with advanced cancer at diagnosis for every 4 patients potentially treated unnecessarily for low-risk disease. Early reports have demonstrated a stage migration following the USPSTF statements toward more advanced disease at diagnosis, thereby increasing the pool of patients with more advanced disease eligible for RP.[21]

PROGNOSIS FOR RELAPSED MEN

BCR can signify cancer in the pelvis (nodal or in the prostatic bed), cancer at a distant site, or the