

Original Article

Salvage radiotherapy for patients with increasing prostate-specific antigen levels after radical prostatectomy: evaluation of the role of retrograde urethrography

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Abstract

Purpose: To evaluate the role of retrograde urethrography in treatment planning for salvage external beam radiotherapy in patients with increasing prostate-specific antigen levels after radical prostatectomy.

Methods and Materials: From July 1988 to December 2002, 173 consecutive patients received external beam radiotherapy for increasing prostate-specific antigen levels after radical prostatectomy. All 173 simulation films were reviewed, and retrograde urethrography was performed in 148 patients (86%). The distance between the line connecting the lower poles of the ischial tuberosities and site of abrupt narrowing of contrast material was measured in all 148 patients. This distance was compared with that measured in 148 consecutive patients with intact prostates who had retrograde urethrography while undergoing treatment planning for definitive radiotherapy.

Results: The mean (median) distance from the line connecting the lower poles of the ischial tuberosities to the abrupt narrowing seen in the urethrogram in patients with increasing prostate-specific antigen levels was 1.54 cm (1.50 cm) compared with 1.73 cm (1.80 cm) in those with intact prostates ($p = 0.0145$).

Conclusion: Retrograde urethrography is important in treatment planning for salvage radiotherapy of the prostate bed after radical prostatectomy to adequately treat the apex of the prostate bed.

Keywords

Prostatectomy; prostate-specific antigen; salvage radiation; urethrography

INTRODUCTION

It was estimated that 232,000 new cases of prostate cancer would be diagnosed in the U.S. in 2005.¹ Radical prostatectomy is selected as initial therapy in approximately one-third of U.S. men with prostate cancer,^{2,3} and it may be used in up to

three-fourths of younger men.² Therefore, more than 75,000 men may undergo radical prostatectomy during 2005, and one-third or more may experience an isolated prostate-specific antigen (PSA) elevation within 5–10 years.^{3–6}

Salvage external beam radiotherapy for an increasing PSA level after radical prostatectomy has been effective for approximately 45% of patients.^{7,8} Many patient- and treatment-related prognostic factors have been reported, including the Gleason score, seminal vesicle involvement,

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postprostatectomy PSA level at the initiation of radiotherapy, surgical margins, PSA doubling time, seminal vesicle involvement, and radiation dose.^{7,8}

Because the apex of the prostate is involved by prostate cancer at the time of radical prostatectomy in 35% of patients,⁹ dose coverage of the apex of the prostate bed is essential. Retrograde urethrography has been demonstrated to be an effective study to evaluate the location of the prostate apex in patients undergoing simulation for prostate cancer.^{10–13} However, retrograde urethrography has not been evaluated in patients receiving salvage radiation for an increasing PSA level after radical prostatectomy. Therefore, we reviewed the urethrograms of all patients who underwent simulation for salvage radiotherapy for an increasing PSA level after radical prostatectomy at Mayo Clinic in Jacksonville.

MATERIALS AND METHODS

From July 1988 to December 2002, 173 consecutive patients received salvage external beam radiotherapy because of increasing PSA levels after radical prostatectomy. Retrograde urethrography was routinely performed as a component of the simulation procedure to assess the location of the prostate apex bed. Simulation films for all 173 patients were reviewed, and 148 patients (86%) had undergone retrograde urethrography. The distance between the line connecting the lower poles of the ischial tuberosities and the site of abrupt narrowing of contrast material was measured in all 148 patients. This line was chosen as a reference line to assess the position of the abrupt narrowing on the retrograde urethrogram. This distance was compared with the distance measured in 148 consecutive patients with an intact prostate who had retrograde urethrography while undergoing treatment planning for definitive radiotherapy alone. We performed this analysis to assess the importance of retrograde urethrography as a component of the treatment planning process in patients recommended to receive salvage radiation for an increasing PSA level after radical prostatectomy.

The radical prostatectomy pathology reports for the 148 patients with increasing PSA levels were reviewed to determine the incidence of positive

margins of the apex of the prostate. The pathology reports were available for 134 (91%) of the 148 patients.

The difference between the 2 groups of patients in the distance from the abrupt narrowing of contrast material to the line connecting the lower poles of the ischial tuberosities was analyzed statistically with the *t* test and analysis of variance. With this sample size, we were able to estimate the sample mean for each group with a 95% confidence interval (CI) ranging from +0.1 to –0.1 cm from the estimate for each group. Statistical significance was determined at the 5% level.

RESULTS

Of the 134 radical prostatectomy pathology reports, 44 (33%) documented that the margins of the apex of the prostate were positive for prostate cancer. Therefore, adequate dose coverage of the apex of the prostate bed was essential for approximately one-third of our patients.

The mean distance from the line connecting the lower poles of the ischial tuberosities to the abrupt narrowing of contrast material seen in the urethrogram in patients with increasing PSA levels was 1.54 cm (95% CI, 1.44–1.64 cm) compared with 1.73 cm (95% CI, 1.62–1.85 cm) for those with intact prostates ($p = 0.015$) (Fig. 1). The *t* test was 2.46 on 294 degrees of freedom. This finding is clinically significant because it demonstrates that the prostate apex bed lies more inferior in the pelvis after radical prostatectomy than it does in patients with an intact prostate. The prostate apex bed must be included in the clinical target volume. Figure 2 is a urethrogram from a patient with an increasing PSA level in whom the tip of the abrupt narrowing of the contrast material was only 2 mm above the line connecting the lower poles of the ischial tuberosities.

DISCUSSION

The role of retrograde urethrography has been evaluated in planning radiotherapy for prostate cancer. Several studies have demonstrated that retrograde urethrography can help prevent a geographic miss of the prostate gland, specifically the apex.^{10–13} The distance from the abrupt narrowing,

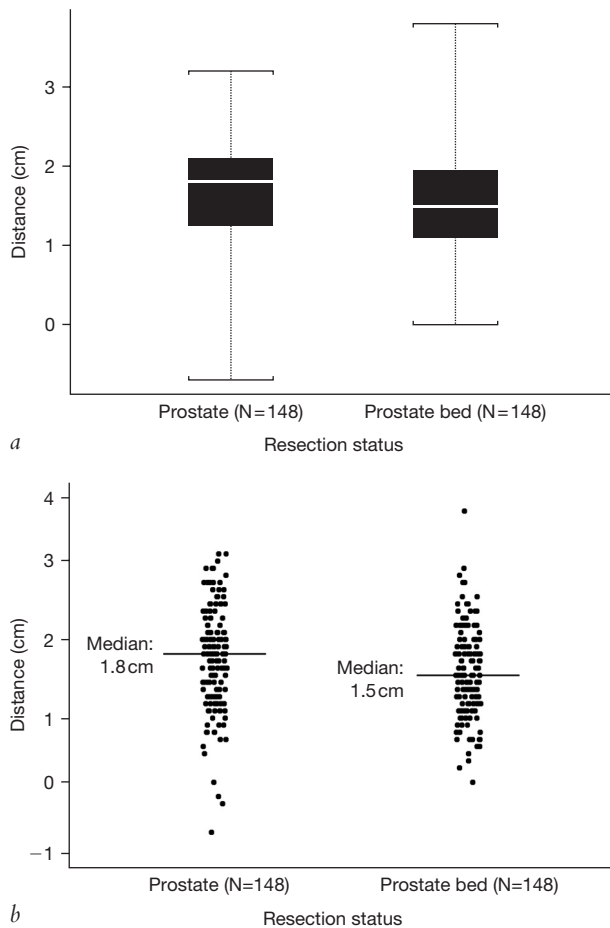


Figure 1. Analysis of distance by resection status. Distance in centimeters from a line connecting the lower poles of the ischial tuberosities with the point of abrupt narrowing of the contrast material seen on a urethrogram. For patients with intact prostates (Prostate), mean = 1.73 cm (95% CI, 1.62–1.85 cm). For patients undergoing salvage prostate bed radiation after radical prostatectomy (Prostate bed), mean = 1.54 cm (95% CI, 1.44–1.64 cm).

or “tip,” seen in the urethrogram to the apex of the prostate, as determined with computed tomography, magnetic resonance imaging, ultrasonography, and plain films of the urethroscope at the external sphincter, is between 5 and 16 mm.^{11,13}

When salvage radiotherapy is administered to the prostate bed for increasing PSA levels after radical prostatectomy, adequate dose coverage of the apex of the prostate bed is essential. In our study, the surgical margins of the apex were positive in 33% of the 134 patients for whom pathology reports were available. One additional report

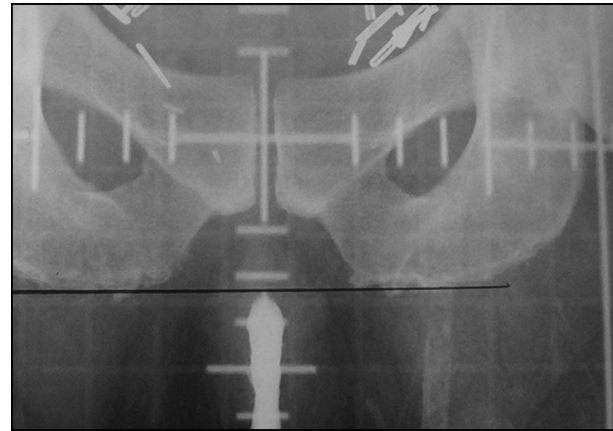


Figure 2. Retrograde urethrogram of patient undergoing radiotherapy for increasing PSA level after radical prostatectomy. The tip of the abrupt narrowing of the contrast material was only 2 mm above the line connecting the poles of the ischial tuberosities.

has documented involvement of the apex of the prostate in 35% of patients.⁹

Because the prostate blends inferiorly with the urogenital diaphragm, the apex cannot be localized precisely with computed tomography.¹³ It is at least as difficult to localize the apex with computed tomography after radical prostatectomy as it is in patients with intact prostates.

In our retrospective study, the mean and median distances from the abrupt narrowing of contrast material in urethrograms to the line connecting the lower poles of the ischial tuberosities were significantly less in the 148 patients who had radical prostatectomy than in the 148 with intact prostates. These data suggest that the apex of the prostate bed may be more inferior in patients after radical prostatectomy than in those with intact prostates. Therefore, it is essential to adequately cover the prostate apex bed. Retrograde urethrograms are an effective method to evaluate this important anatomical site.

Each year a substantial number of men experience an increasing PSA level after prostatectomy.¹⁴ The majority of these men are candidates for radiotherapy to the prostate bed. In addition, a prospective randomized trial of patients with pathologic stage T3 disease after radiotherapy demonstrated statistically significant improvement

in biochemical and clinical progression-free survival of patients who received radiotherapy post-operatively.¹⁵

Two Radiation Therapy Oncology Group (RTOG) randomized studies are evaluating the use of adjuvant and salvage radiotherapy in patients after radical prostatectomy. Both RTOG 96-01 (salvage radiotherapy) and RTOG P-0011 (adjuvant radiotherapy) require retrograde urethrography as part of the treatment planning process.

CONCLUSIONS

Salvage prostate bed radiotherapy is the only salvage therapy that can potentially result in long-term freedom from PSA and clinical progression. Because prostate apex margins are positive in up to 35% of radical prostatectomy specimens, coverage of the prostate apex bed is essential. This study demonstrated that after radical prostatectomy the prostate apex bed may be more inferior in the pelvis than that of an intact prostate. Therefore, the use of retrograde urethrography in planning radiotherapy for these patients may help to prevent a “geographic miss.”

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