Penile Length Changes in Men Treated With Androgen Suppression Plus Radiation Therapy for Local or Locally Advanced Prostate Cancer

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Purpose: We determined penile length alterations in men treated with androgen suppression plus radiation therapy for local or locally advanced prostate cancer.

Materials and Methods: From November 2000 to November 2005, 47 patients were enrolled in this prospective study. After clinical staging all patients received hormonal therapy (luteinizing hormone releasing agonist, leuprolide acetate or goserelin every 3 months for a total of 3 injections) and at month 7 of hormonal therapy radiation therapy was begun (total 70 Gy) for 7 weeks. Stretched penile length measurements were performed before starting androgen suppression therapy and every 3 months thereafter with a paper ruler.

Results: With the initiation of therapy a gradual decrease in stretched penile length was observed. Penile shortening was statistically significant at a mean followup of 18 months (mean 14.2 to 8.6 cm, $p < 0.001$).

Conclusions: Our findings support observations of decreased penile length after neoadjuvant hormonal therapy plus external beam radiation therapy for local or locally advanced prostate cancer. Patients should be counseled before therapy that penile shortening may occur.

Key Words: organ size, radiotherapy, prostatic neoplasms

With the advent of prostate specific antigen, many cases of prostate cancer are being diagnosed as localized[1] and are treated with radical prostatectomy or radiotherapy.[2] On the other hand, for locally advanced prostate cancer radiotherapy combined with hormone therapy is generally the accepted form of treatment.[3,4] Many of these patients can be cured and, moreover, there is an increasing number of patients who can expect to survive for long periods after treatment. Thus, disease specific quality of life after treatment has become an important issue in this patient population. Erectile dysfunction is a potential side effect of radiation therapy that may adversely impact quality of life.[5] Additionally, some patients have reported that the penis is smaller after radiotherapy. However, to our knowledge no prospective study has been conducted to evaluate stretched penile length changes after hormonal therapy plus radiotherapy for localized or locally advanced prostate cancer. We conducted a prospective study to determine penile length alterations after this therapy for prostate cancer.

PATIENTS AND METHODS

From November 2000 to November 2005, 47 patients were enrolled in this prospective study to evaluate penile length changes following neoadjuvant hormonal therapy plus radiation therapy for prostate cancer. Eligible patients included those with a prostate specific antigen of at least 10 ng/ml (maximum 40 ng/ml) and an Eastern Cooperative Oncology Group performance status of 0 or 1. All Gleason scores were acceptable. Clinical stage ranged from T2 to T3b (TNM 1997). All patients were required to have a negative bone scan and pelvic lymph node assessment using a computerized tomography scan of the abdomen and pelvis. Normal baseline hepatic and renal function were required, plus an estimated life expectancy of more than 5 years. All patients provided oral and/or written informed consent.

Hormonal Therapy

Luteinizing hormone releasing hormone agonist (leuprolide acetate or goserelin) was injected intramuscularly (leuprolide acetate) or subcutaneously (goserelin) every 3 months for a total of 3 injections. Bicalutamide was begun orally at 50 mg per day 10 days before the initiation of the luteinizing hormone releasing hormone agonist injections and discontinued 10 days after the injections.

Radiation Therapy

Photons of 10 MV were used. Patients were treated once daily, 5 days each week for 7 weeks. The daily dose was 2 Gy. Thus, patients received a total dose of 70 Gy using a 2-phase 4-field approach. Small fields were used to treat the prostate

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and the seminal vesicles to a dose of 50 Gy with a boost to the prostate alone to the total dose during 7 weeks. Radiation therapy was to begin at month 7 of hormonal treatment.

At baseline and after the administration of AST, a complete blood cell count and liver function tests were obtained monthly until the 9-month course of AST was complete. Stretched penile length measurements were performed before starting AST and every 3 months thereafter by the same physician (AHH) with a paper ruler. Stretched penile length was measured from the tip of the glans to the pubopenile skin junction while applying tension to maximally stretch the penis.

The difference between penile length measurements before and after treatment were evaluated using the Bonferroni corrected Wilcoxon signed rank test, and $p < 0.05$ indicated statistically significant differences. The difference between 2 groups in terms of penile stretched length (less than 14 vs 14 cm or greater) at 12 months was evaluated with the Mann-Whitney U test.

RESULTS

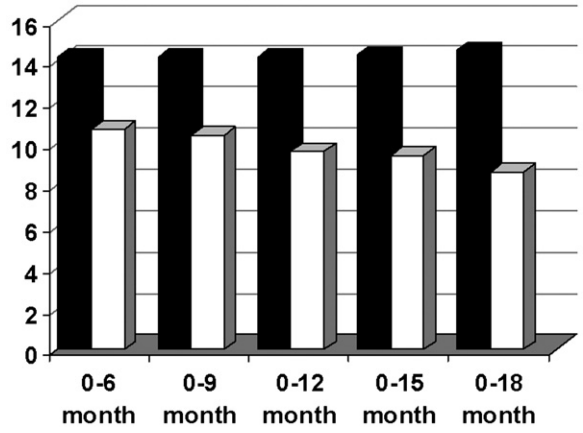
Mean patient age was 68.8 years (range 50 to 79). No patient had a penile abnormality (eg Peyronie's disease) or a history of penile or urethral surgery. Mean followup was 18 months (range 9 to 57). Before therapy the median value for stretched penile length was 14.0 cm (range 11 to 17, 14.20 ± 1.10). With the initiation of therapy a gradual decrease in stretched penile length was observed until 18 months (see table). A significant correlation existed between baseline length and percentage of penile shortening ($p < 0.001$). At 12 months patients whose baseline penile length was less than 14 cm had a significantly lower percentage of shortening than those with a baseline of 14 cm or greater, $p = 0.01$ (less than 14 cm, median decrease −24%; 14 cm or greater, median decrease −35.7%).

The figure shows the alterations in penile length. Of the patients 23.04% indicated normal erectile function before therapy and 12.5% reported erections sufficient for intercourse at the 18-month followup. Erectile function was assessed with the International Index of Erectile Function symptom score.

DISCUSSION

Quality of life concerns are important when considering treatment options for prostate cancer.[6] Sexual dysfunction is a potential side effect of radical retropubic prostatectomy and radiotherapy that may adversely impact quality of life.[5,7] In addition to erectile dysfunction Savoie et al and Munding et al reported 68% and 71% penile length decrease after radical retropubic prostatectomy at 3 months of followup, respectively.[8,9] The mechanisms responsible for the reduction in stretched penile length after radical retropubic prostatectomy have not been characterized, although different hypotheses have been proposed such as postoperative denervation atrophy and/or fibrosis of the penile cavernous smooth muscle.[10] Klein et al showed that apoptosis of penile erectile tissue after cavernous neurotomy in rats is a possible explanation for decreased penile size following radical prostatectomy.[11] Some of these hypotheses might also account for the penile length changes we observed in our prospective study.

The combination of radiotherapy and hormone therapy is an effective treatment alternative for locally advanced prostate cancer, but it has also been shown that sexual problems, mainly erectile dysfunction, are worse in patients who have received combined radiation/hormone treatment compared with controls.[12] As with radical retropubic prostatectomy, a complaint we received from our patients after combined radiation/hormone treatment is that the penis was shortened. Although erectile dysfunction is a potential side effect of radiotherapy and combined radiation/hormone treatment, to our knowledge no prospective study has been conducted to evaluate stretched penile length changes after hormone therapy plus radiotherapy. Although Hashine et al reported that a combination of radiotherapy and hormone therapy has a good outcome except for sexual problems, they did not mention penile length changes.[12] In our study group penile length decreased from a mean of 14.5 to 8.6 cm (41% decrease) at 18 months. Because these patients were initially treated with 9 months of hormonal therapy, this might have an effect on penile length as hormonal therapy is also strongly associated with erectile dysfunction. However, we can also speculate that penile length changes might be the long-term inflammatory microvessel changes and neural injuries that occur after external beam radiotherapy.[5] More recent evidence has implicated structural alterations in corporeal smooth muscle as potential contributors to erectile dysfunction and possibly to penile length decrease.[13] It has also been shown that men presenting with erectile dysfunction after radiation therapy for prostate cancer are likely to



Mean stretched penile length values before (black bars) and after (white bars) therapy.

Stretched penile length measurement results

Mos	No. Evaluated	Mean (cm)	SD	Median (cm)	Min (cm)	Max (cm)
0	47	14.20	1.10	14	11	17
6	47	10.70	1.03	11	8	13
0	47	14.20	1.10	14	11	17
9	47	10.40	1.04	10	8	13
0	39	14.26	1.12	14	11	17
12	39	9.60	1.20	9	7.4	13
0	35	14.35	0.91	14	13	17
15	35	9.40	1.33	9	8	13
0	24	14.51	0.93	14.20	13	17
18	24	8.60	1.06	8	7	11

All values $p < 0.001$.

have significant alterations in erectile hemodynamics, often of a combined arteriovenogenic nature,[5] and this may also have an effect on penile length changes. Generally doses greater than 20 Gy are required to induce large vessel injury and our patients received a dose of 70 Gy, well in excess of the dose required for arterial injury. Those patients with a longer baseline penile length (14 cm or greater) tended to have a greater decrease in length. Despite our findings this study is limited by a relatively small sample size. We are following these patients to determine if longer followup will reveal further change in penile size.

CONCLUSIONS

Our findings support observations of decreased penile length after neoadjuvant hormonal therapy plus external beam radiation therapy for local or locally advanced prostate cancer. Patients should be counseled before this therapy that penile shortening may occur.

Abbreviations and Acronyms

AST = androgen suppression therapy

REFERENCES

1. Egava S, Matsumoto K, Yoshida K, Iwamura M, Kuwao S and Koshiba K: Results of transrectal ultrasound-guided biopsies and clinical significance of Japanese prostate cancer. Jpn J Clin Oncol 1998; **28:** 666.
2. Cooperberg MR, Broering JM, Litwin MS, Lubeck DP, Mehta SS, Henning JM et al: The contemporary management of prostate cancer in the United States: lessons from the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE), a national disease registry. J Urol 2004; **171:** 1393.
3. Bolla M, Collette L, Blank L, Warde P, Dubois JB, Mirimanof RO et al: Long-term results with immediate androgen suppression and external irradiation in patients with locally advanced prostate cancer (an EORTC study) a phase III randomized trial. Lancet 2002; **360:** 103.
4. Roach M 3rd, DeSilvio M, Lawton C, Uhl V, Machtay M, Seider MJ et al: Phase III trial comparing whole-pelvic versus prostate-only radiotherapy and neoadjuvant versus adjuvant combined androgen suppression: Radiation Therapy Oncology Group 9413. J Clin Oncol 2003; **21:** 1904.
5. Raina R, Agarwal A, Goyal KK, Jackson C, Ulchaker J, Angermeier K et al: Long-term potency after iodine-125 radiotherapy for prostate cancer and role of sildenafil citrate. Urology 2003; **62:** 1103.
6. Bokhour BG, Clark JA, Inui TS, Silliman RA and Talcott JA: Sexuality after treatment for early prostate cancer: exploring the meanings of "erectile dysfunction." J Gen Intern Med 2001; **16:** 649.
7. Penson, DF and Litwin, MS: Quality of life issues in patients with prostate cancer. AUA Update Series 2001; **20:** lesson 3.
8. Savoie M, Kim SS and Soloway MS: A prospective study measuring penile length in men treated with radical prostatectomy for prostate cancer. J Urol 2003; **169:** 1462.
9. Munding MD, Wessells HB and Dalkin BL: Pilot study of changes in stretched penile length 3 months after radical retropubic prostatectomy. Urology 2001; **58:** 567.
10. McCullough AR and Lepor H: The loss of penile length and circumference in impotent men after nerve sparing radical prostatectomy. J Urol, suppl., 1998; **159:** 98, abstract 376.
11. Klein LT, Miller MI, Buttyan R, Raffo AJ, Burchard M, Devris G et al: Apoptosis in the rat penis after penile denervation. J Urol 1997; **158:** 626.
12. Hashine K, Azuma K, Koizumi T and Sumiyoshi Y: Health-related quality of life and treatment outcomes for men with prostate cancer treated by combined external-beam radiotherapy and hormone therapy. Int J Clin Oncol 2005; **10:** 45.
13. Hall SJ, Basile G, Bertero EB, de las Morenas A and Goldstein I: Extensive corporeal fibrosis after penile irradiation. J Urol 1995; **153:** 372.