Testosterone Therapy and Risk of Recurrence After Treatment for Prostate Cancer

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Clinical Question
In patients who are presumed cured of organ-confined prostate cancer, what are the benefits of testosterone replacement therapy, and what is the risk of cancer recurrence?

Evidence-Based Answer
Men with symptomatic androgen deprivation who have had clinically curative treatment for organ-confined prostate cancer may have symptomatic improvement with testosterone replacement therapy. (Strength of Recommendation [SOR]: C, based on two small case series.) There are no studies evaluating the risk of cancer recurrence in patients receiving testosterone replacement therapy. However, testosterone replacement therapy may be associated with increased prostate-specific antigen (PSA) levels. (SOR: C, based on one case report.) Some men discontinue therapy because their symptoms do not improve. (SOR: C, based on a small case series.)

Evidence Summary
Seven case series (n = 206 patients) describe symptomatic improvements in men with androgen deprivation syndrome who received testosterone replacement therapy.1-7 PSA levels were monitored over periods ranging from six months to 12 years. All of the case series included men who received clinically curative therapy for organ-confined prostate cancer; five used radical prostatectomy,1-5 one used brachytherapy,6 and one used external beam radiotherapy.7 (Table 11-4,6,7).

Two case series evaluated androgen deprivation symptoms in patients receiving testosterone replacement therapy.2,7 The first study included 10 men (average age = 54 years) who used the hormonal assessment subscale of the Expanded Prostate Cancer Index Composite.2 This self-administered quality-of-life questionnaire measures hot flashes, breast tenderness, depression, low energy, and weight change. On a scale of 0 (no improvement) to 100 (maximum improvement), scores for patients receiving testosterone replacement therapy improved from 38 (95% confidence interval [CI], 32 to 46) to 49 (95% CI, 46 to 54). The second study described five men (average age = 66 years) who had 30 androgen-related symptoms (e.g., hot flashes, decreased libido, erectile dysfunction, lack of ejaculation, fatigue, muscle aches, depressed mood).7 After testosterone replacement therapy, the men had only 14 symptoms.

No studies have evaluated the risk of cancer recurrence after testosterone replacement therapy. The seven case series discussed above monitored PSA levels and found one patient with an unexpected increase.1-7 The authors did not describe a clinical recurrence of cancer in that case. In one case series, five of 36 patients discontinued therapy because of a lack of perceived symptomatic benefit, and one patient reported headache.6

Recommendations from Others
A 2008 consensus guideline from the International Society of Andrology, International Society for the Study of the Aging Male, European Association of Urology, European Academy of Andrology, and American Society of Andrology states that men successfully treated for prostate cancer who have confirmed symptomatic hypogonadism are candidates for testosterone replacement therapy if there

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is no clinical or laboratory evidence of residual cancer. It states that physicians should discuss the risks and benefits of therapy with the patient and ensure close follow-up. The Endocrine Society recommends against initiating testosterone replacement therapy in this population.

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REFERENCES


Table 1. Case Series Using Testosterone Replacement Therapy After Clinically Curative Therapy for Organ-Confined Prostate Cancer

<table>
<thead>
<tr>
<th>Case series</th>
<th>Definitive therapy</th>
<th>Baseline Gleason score</th>
<th>Mean/median follow-up (range)</th>
<th>Normal serum testosterone level achieved?</th>
<th>Outcomes</th>
<th>Recurrence (based on PSA level)</th>
</tr>
</thead>
</table>
| Kaufman (2004)<sup>1</sup>  

n = 7; mean age = 64 years  

Radical prostatectomy  

6 1 0  

18 months (6 months to 12 years)  

Yes: 6  

Unknown: 1  

3 participants reported symptom improvement  

None  

Agarwal (2005)<sup>2</sup>  

n = 10; mean age = 54 years  

Retroperitoneal radical prostatectomy  

2 7 1  

19 months (NA)  

Yes: 10  

Decreased hot flashes, increased energy  

None  

Nabulsi (2008)<sup>3</sup>  

n = 22; mean age = 61 years  

Radical prostatectomy  

13 7 2  

24 months (14 to 30 months)  

Yes: 22  

Not reported  

1 (Gleason score = 8)  

Khera (2009)<sup>4</sup>  

n = 57; mean age = 64 years  

Radical prostatectomy  

24 26 4  

13 months (7 to 17 months)  

Yes: 57  

Not reported  

None  

Sarosdy (2007)<sup>6</sup>  

n = 36; mean age = 65 years  

Brachytherapy (with or without external beam radiotherapy)  

22 6 3  

4.5 years (1.5 to 9 years)  

Yes: 31  

5 participants discontinued therapy because of no perceived benefit  

None  

Morales (2009)<sup>7</sup>  

n = 5; mean age = 66 years  

External beam radiotherapy  

2 1 2  

15 months (6 to 27 months)  

Unknown: 5  

4 participants reported decreased hot flashes, improved libido, and increased energy  

2 participants had improved erectile function  

Final PSA level <1.5 ng per mL (1.5 µg per L)  

NA = not available; PSA = prostate-specific antigen.

Information from references 1 through 4, 6, and 7.