FPIN's Clinical Inquiries

Testosterone Therapy and Risk of Recurrence After Treatment for Prostate Cancer

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Clinical Inquiries provides answers to questions submitted by practicing family physicians to the Family Physicians Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (http://www.cebm.net/?o=1025).

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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 1[1-4,6,7])*.

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

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

Case series	Definitive therapy	Baseline Gleason score ≤6	7	≥8	Mean/median follow-up (range)	Normal serum testosterone level achieved?	Outcomes	Recurrence (based on PSA level)
Kaufman (2004)[1] 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)[2] 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)[3] 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)[4] n=57; mean age=64 years	Radical prostatectomy	24	26	4	13 months (7 to 17 months)	Yes: 57	Not reported	None
Sarosdy (2007)[6] 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)[7] 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.

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.[8] The Endocrine Society recommends against initiating testosterone replacement therapy in this population.[9]

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