An Evidence Based Approach to Testosterone Replacement Therapy in Patients with Prostate Cancer or BPH

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Objectives:
• Describe the risk of testosterone replacement therapy in patients with prostate cancer
• Discuss the risks of testosterone replacement therapy in patients with BPH
• Develop a practical algorithm for selecting, treating and monitoring patients with prostate cancer and/or BPH who also require testosterone replacement therapy
Testosterone Replacement Therapy: Safety Issue Update

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Declarations

- None
Review Safety Issues Related to TRT

- Prostate cancer
  - Incident disease
  - Active surveillance
  - After definitive treatment (surgery or radiation)

- Lower urinary tract symptoms (LUTS)

- Non-urological conditions
TRT and Incident Prostate Cancer

- There is no conclusive evidence that TRT increases the risk of incident prostate cancer.
  - Based on Level 2 evidence of serum testosterone and prostate cancer risk.
  - No Level 1 evidence (nor will there ever be).

### Testosterone and Prostate Cancer

18 Studies, 3886 men

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<th>No. of case patients/No. of control subjects</th>
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TRT and Incident Prostate Cancer

- There is no evidence that TRT will convert subclinical prostate cancer into a more aggressive phenotype.

- There is evidence that exogenous testosterone will stimulate growth and symptoms in locally advanced and metastatic cancer.

  - Fowler JE et al. *Cancer* 1982
Testosterone and Metastatic Prostate Cancer

Considerations for the Use of Testosterone with Systemic Chemotherapy in Prostatic Cancer

JACKSON E. FOWLER, JR., MD,* AND WILLET F. WHITMORE, JR., MD†

- n = 52 men with metastatic disease given testosterone
- 89% experienced clinical exacerbations
  - Bone pain, anoxeria, increased acid phosphatase, and death

Fowler JE et al. Cancer 1982
Screening Prior to TRT
Evidence-Based Recommendations

- Is there a need to screen prior to treatment?

- Official recommendation: Yes.
  - PSA, DRE, risk stratification tools.

Is this recommendation outdated? Possibly.
Screening Prior to TRT
Bottom Line

• But the evidence-based guidelines and FDA statements are unequivocal.
  • Screening is indicated prior to treatment.
  • If patient declines, documentation of informed discussions of risks and benefits is essential.

There are no clinical data on which to base recommendations for TRT in patients with localized, low risk prostate cancer on active surveillance.
TRT and Active Surveillance

• Evidence-based guidelines do not offer recommendations.
  • Presumably because TRT in patients with untreated prostate cancer is contraindicated.

TRT and Active Surveillance

• But there is no evidence that TRT will convert low risk prostate cancer into a more aggressive phenotype.

  and

• There is a high prevalence of undiagnosed, clinically insignificant prostate cancer in older U.S. men.

• Untreated prostate cancer remains a contraindication to TRT.

• TRT in appropriate patients with untreated prostate cancer on AS is probably safe.
  • But if TRT is initiated, documentation of informed discussions of risks and benefits is essential.
TRT After Definitive Treatment
Evidence-Based Guidelines

• Men with localized disease successfully treated are potential candidates for TRT:
  • If no clinical or laboratory evidence of disease.
  • Following a “prudent” disease-free interval.
    • Length of interval undefined.

TRT After Definitive Treatment

• Several cohort studies support the safety of TRT after:
  • Radical prostatectomy\(^1,2\)
  • Brachytherapy\(^3,4\)
  • External beam radiotherapy\(^4,5,6\)

6. BJU Int. 2010 May;105(10):1397-401
TRT After Definitive Treatment

• These were small series with very limited power.

• Consistent PSA rises were observed in all 3 treatment groups after TRT.
  • Minority of patients.
  • Not always associated with progression.
TRT After Definitive Treatment

Bottom Line

• TRT in appropriate patients is probably safe.

• Close attention on follow-up is indicated.

• Document disease-free state.
  • Radical prostatectomy: PSA < 0.01 ng/mL
  • Radiotherapy: RTOG-ASTRO criteria
TRT After Definitive Treatment
Bottom Line

- Begin TRT once patient is disease-free.

- Discontinue if biochemical recurrence
  - Radical prostatectomy: PSA > 0.1 ng/mL
  - Radiotherapy: >2.0 ng/mL from nadir

- Documentation of informed discussions of risks and benefits is essential.
TRT and LUTS

- Severe LUTS (I-PSS ≥ 20) is a relative contraindication to TRT.
  - Consider evaluation for and treatment of bladder outlet obstruction first.
  - After treatment, this contraindication is not applicable.

TRT and LUTS

• But there are no data to suggest that TRT
  • Worsens LUTS
  • Causes urinary retention
  • Promotes clinically significant prostate growth

• Small cohort studies have observed no links between LUTS and TRT

• Yassin DJ et al. World J Urol 2013 Oct 18
• Pearl JA et al. J Urol. 2013 Nov;190(5):1828-33
TRT and LUTS

- In fact, there is growing evidence that TRT might *improve* LUTS.
  - Decreased serum testosterone increases LUTS.
  - Androgen deprivation increases LUTS.
  - At least one study shows decreased LUTS with TRT.

- Trifiro MD et al. BJU Int. 2010 Jun;105(11):1554-9
- Parsons JK et al. J Urol. 2010 Sep;184(3):1040-4
- Yassin DJ et al. World J Urol 2013 Oct 18
TRT and LUTS
Bottom Line

• TRT is safe with respect to LUTS.

• There is no compelling evidence to suggest it will clinically worsen LUTS or BPH.
  • There is some evidence (Level IIb and III) suggesting it will improve symptoms.
TRT and Non-urological Conditions

- TRT should not be started in men with the following conditions:
  - Erythrocytosis > 52%
  - Untreated obstructive sleep apnea
  - Untreated severe congestive heart failure

### TRT and Erythrocytosis Monitoring During TRT

- Erythrocytosis may develop during treatment.

- Perform CBC:
  - Before treatment
  - Every 3-4 months during 1st year
  - Annually thereafter

- Discontinue if Hct 52-55% and coordinate with PCP

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*Wang C et al. Euro Urol 2009 (55) 121-30*
TRT and Non-Urological Conditions

Bottom Line

• Consider non-urological conditions before TRT.
  • Erythrocytosis
  • Sleep apnea
  • CHF

• Regularly monitor CBC

• Coordinate with primary physician as needed