Hypogonadism

Evaluation Management and Treatment Considerations

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KEYWORDS

• Hypogonadism • Testosterone replacement therapy • Metabolic syndrome
• Prostate cancer • Physician assistant

KEY POINTS

- There is an increase in the prevalence of hypogonadism in both younger and older men.
- The evaluation of men with hypogonadism is often poorly understood, leading to suboptimal treatment.
- Hypogonadism has been shown to be associated with cardiometabolic disease and, therefore, requires a thorough evaluation that addresses the various associated comorbidities.
- Controversies related to the treatment of hypogonadism in men with prostate cancer remains a topic of much debate.
- Large randomized controlled trials will need to be conducted to provide clinicians with the most accurate evidence regarding the safety of testosterone replacement therapy (TRT) and the impact of TRT on alleviating or controlling associated comorbidities.

INTRODUCTION

Hypogonadism, also referred to as testosterone deficiency, is defined as a decrease in the concentration of serum total testosterone (<300 ng/dL) and/or a decrease in sperm production.[1] Signs and symptoms include decreased libido, fatigue, erectile dysfunction, loss of body and facial hair, decreased bone mineral density, increased body fat, decreased lean muscle mass, weakness, depressed mood, sleep disturbance, and anemia. The prevalence of hypogonadism in men aged 45 years or older visiting primary care practices in the United States is estimated to be approximately 38.7%.[2] Further evidence indicates there is a higher prevalence of hypogonadism in men with obesity, diabetes, hypertension, rheumatoid arthritis, hyperlipidemia, and osteopenia or osteoporosis.[2] Conflicting evidence on the prevalence of hypogonadism

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combined with the constellation of symptoms can lead to suboptimal evaluations of men presenting with testosterone deficiency. Most clinicians follow the guidelines established by the Endocrine Society; however, the American Association of Clinical Endocrinologists Guidelines, and the *International Society for Sexual Medicine's Process of Care for the Assessment and Management of Testosterone Deficiency in Adult Men* can make it difficult to reach a consensus on the best practice approach for the evaluation, treatment, and management of hypogonadism in men.[3]

EVALUATION OF HYPOGONADISM

Initial evaluation of men with hypogonadism presenting with 1 or more objective symptoms (**Table 1**) should begin with a comprehensive history and identification of potential comorbidities associated with hypogonadism (**Table 2**). A thorough physical examination should include identifying the presence of gynecomastia, the presence of secondary sex characteristics (decreased body hair [pubic or axillary], decreased beard growth), a testicular examination paying close attention to the size and consistency of the testicles (adult testes are usually between 20 and 30 mL in volume and from 4.5 to 6.5 cm long by 2.8–3.3 cm wide), prostate examination, and body mass index (BMI).[1,4] Laboratory testing parameters vary between the published guidelines; however, all agree that measurement of a morning total testosterone level by a reliable assay and confirmed by repeat measurement should be obtained to confirm the diagnosis. Men with total testosterone near the lower limit of normal or in men in whom sex hormone-binding globulin abnormality is suspected (eg, older men, men with obesity, diabetes mellitus, chronic illness, liver disease, or thyroid disease) should have additional laboratory testing performed (**Table 3**). Further laboratory testing should include serum luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels to distinguish between primary (testicular) and secondary (pituitary-hypothalamic) hypogonadism. Measurement of LH and FSH concentrations can help distinguish between primary and secondary hypogonadism. Men with primary hypogonadism have low testosterone levels with elevated LH and FSH levels, whereas men with secondary hypogonadism have low testosterone levels with low or normal LH levels. Serum LH levels in men with secondary hypogonadism may be below the normal range or in the low-normal range but clearly inappropriate in relation to the low testosterone

Table 1
Clinical presentation of hypogonadism

Physical	Psychological	Sexual
Decreased bone mineral density	Diminished energy, sense of vitality, or well-being	Decrease spontaneous directions
Decrease muscle mass and strength	Impaired cognition and memory	Erectile dysfunction
Gynecomastia	Decreased mood	Difficulty achieving orgasm
Anemia		Diminished libido
Frailty		
Increased body mass index		
Fatigue		
Insulin resistance		
Enlarged liver or elevated liver function tests		

Data from Refs.[1,4,5]