

Updated Review on Surgical Management of Male Hypogonadism

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ABSTRACT

In this review, we discuss the treatment options for male hypogonadism and the associated benefits and potential short- and long-term risks. The choice for treatment may depend on the cause of hypogonadism and the desire for maintaining or improving fertility. We also highlight surgical management of male hypogonadism. Comprehensive searching strategy through Well-known medical databases (MIDLINE/ PubMed, and Embase) searching articles that published in English language up to December 2017, and discussing the surgical management of male hypogonadism. Male hypogonadism is identified by the presence of symptoms or signs of male hypogonadism and consistent serum testosterone levels that are below the normally accepted adult male range. Once the medical diagnosis is confirmed, the primary goal of treatment is testosterone substitution to accomplish serum testosterone levels that remain in the mid-adult range and the symptoms and signs of hypogonadism are eliminated. Recent developments led to numerous delivery systems for testosterone. For patients with primary hypogonadism testosterone therapy is the approach of choice. The patient needs to be completely informed about expected benefits and side-effects of the treatment option. The option of the preparation should be a joint decision by a notified patient and the doctor.

Keywords: **surgical management , male,hypogonadism.**

INTRODUCTION

Male hypogonadism is defined as the failing to generate sufficient flowing testosterone and/or spermatozoa in the ejaculate, resulting in symptoms and signs of testosterone deficiency and/or infertility^[1]. Male hypogonadism needs to be identified and treated, since when neglected, hypogonadal men may develop a clinical disorder of lowered sexual function, infertility, tiredness, damaged sense of well-being, anemia, decreased bone density, decreased lean body mass (LBM) and muscle strength, as well as enhanced fat mass and visceral adiposity, which might be associated with metabolic disorder^[1,2]. The reduced practical capability of the testis to produce adequate amounts of testosterone and/or mature spermatozoa can be due to issues in the testis, pituitary and/or hypothalamus, or at numerous degrees.

Primary hypogonadism results from disorders of the testes that result in low testosterone production and damaged spermatogenesis. The more typical causes of primary hypogonadism or hypergonadotrophic hypogonadism consist of chromosomal defects (e.g., Klinefelter syndrome), testicular injury (e.g., chemotherapy, radiation, surgical procedure, trauma) and infection. The occurrence of Klinefelter syndrome is thought to be in between 0.15 and 0.2% in males^[3].

The frequency of hypogonadism due to genetic or idiopathic problems in the pituitary or hypothalamus is

unusual in clinical practice except in tertiary referral centers. Hypogonadotrophic hypogonadism could be because of congenital and/or acquired problems. Congenital hypogonadotrophic hypogonadism can occur as a result of problems in gonadotropin releasing hormone (GnRH) nerve cells, GnRH controlling neurons, luteinizing hormone (LH) and follicle stimulating develop (FSH) secreting cells.

These could include genetics anomalies that affect the movement of GnRH nerve cells (e.g., Kallmann syndrome) and mutations in genes that impact signals regulating GnRH neurons.

Separated hypogonadotrophic hypogonadism could also take place due to focal flaws in LH and FSH secreting cells. Obtained problems can develop from architectural defects or reversible reasons. Acquired architectural defects can include damage of GnRH nerve cells (e.g., meningioma, craniopharyngioma, vascular injury), tumors in the pituitary or suprasellar region that hinders typical transportation of hypothalamic releasing or hindering variables getting to the pituitary, damages from trauma or radiation, infections (e.g., abscesses, tuberculosis) and infiltrative illness that impact the hypothalamus and pituitary (e.g., sarcoidosis, hemochromatosis).

Potentially relatively easy to fix causes of hypogonadotrophic hypogonadism could include medications (e.g., metoclopramide, opioids, GnRH agonists and villains), acute systemic ailment, chronic

systemic disease, kind 2 diabetic issues mellitus and weight problems. Mixed (mixed primary and second) hypogonadism can result from dual problems in the testes and in the pituitary-hypothalamic axis, with examples include aging, HIV infection and hemochromatosis.^[7]

In this review, we discuss the treatment options for male hypogonadism and the associated benefits and potential short- and long-term risks. The choice for treatment may depend on the cause of hypogonadism and the desire for maintaining or improving fertility. We also highlight surgical management of male hypogonadism.

METHODOLOGY

Comprehensive searching strategy through Well-known medical databases (MIDLINE/ PubMed, and Embase) searching articles that published in English language up to December 2017, and discussing the surgical management of male hypogonadism. Furthermore, references list of each article were searched for more eligible papers for present review.

The study was done after approval of ethical board of Prince Sattam Bin Abdulaziz university.

DISCUSSION

• **Epidemiology**

Definition: male hypogonadism is a clinical syndrome brought on by androgen deficiency which might adversely influence numerous body organ functions and quality of life (QoL) ^[12]. Androgen deficiency boosts a little with age additionally in healthy males ^[4,5]. In middle-aged males, the occurrence of biochemical hypogonadism varies from 2,1-12.8% ^[6]. The incidence of reduced testosterone and signs and symptoms of hypogonadism in men aged 40-79 varies type 2.1-5.7% ^[6]. Hypogonadism is a lot more prevalent in older men, in males with weight problems, those with co-morbidities, and in men with a poor health and wellness condition.

• **Role of testosterone for male reproductive health**

Androgens, which are produced by the testis and by the adrenal glands, play a crucial duty in male reproductive and sexual function. Androgens are crucial for the advancement of male reproductive body organs, such as the epididymis, vas deferens, seminal vesicle, prostate and penis. Additionally, androgens are needed for puberty, male fertility, male sexual function, muscle formation, body structure, bone

mineralisation, fat metabolism, and cognitive functions ^[7].

• **Aetiology**

Hypogonadism results from testicular failure, or is due to the disruption of one or several levels of the hypothalamic-pituitary-gonadal axis .Male hypogonadism can be classified in accordance with disturbances at the level of:

- the testes (primary hypogonadism);
- the hypothalamus and pituitary (secondary hypogonadism);
- the hypothalamus/pituitary and gonads (hypogonadism in adult men);
- androgen target organs (androgen insensitivity/resistance

• **Clinical symptoms ^[14] :**

Table 1. Clinical symptoms and signs suggestive for androgen deficiency

Delayed puberty	Visceral obesity
Small testes	Reduced sexual desire and sexual activity
Male-factor infertility	Erectile dysfunction
Decreased body hair	Fewer and diminished nocturnal erections
Gynaecomastia	Hot flushes
Decrease in lean body mass and muscle strength	Decrease in bone mineral density (osteoporosis) with low trauma fractures
Changes in mood, fatigue and anger	Sleep disturbances
Metabolic syndrome	Insulin resistance and type 2 diabetes mellitus
Diminished cognitive function	

The most prevalent symptoms of male hypogonadism in aging males are reduced libido and sexual activity, erectile dysfunction, and hot flushes ^[8]. Other aspects found connected with reduced testosterone were midsection circumference and health and wellness standing ^[6]. Signs and symptoms of androgen deficiency differ depending on age of start, duration and the seriousness of the deficiency. Recommendation varies for the reduced typical degree of testosterone (2.5%) have recently been assembled from three large community-based examples, suggesting a cut-off of 12.1 nmol/L for total serum testosterone and for free testosterone 243 pmol/L, to

distinguish between typical levels and levels perhaps associated with deficiency^[9]. Signs suggesting the existence of hypogonadism^[8] are summarised in Table 1. It ought to nevertheless be noted that these signs are likewise discovered in men with regular testosterone levels and could have various other reasons compared to androgen shortage. In guys aged 40-79 years, the threshold for overall testosterone was 8 nmol/L for reduced frequency of sex-related ideas, 8.5 nmol/L for impotence, 11 nmol/L for decreased frequency of early morning erections and 13 nmol/L for decreased vigour^[7].

The strongest forecaster for hypogonadism in this age was 3 sexual signs and symptoms (decreased sexual thoughts, compromised early morning erections, erectile dysfunction) and either an overall testosterone level of < 8 nmol/L or serum testosterone in the range of 8-11 nmol/L and free testosterone < 220 pmol/L. These information are based upon product examples taken in the early morning, when mean levels are highest possible and most reproducible in younger men^[10]. Both immunoassay and mass spectrometry based assays could generate valid results, as long as they are well-validated. Evaluation must be based on recommendation ranges for typical guys given by the research laboratory measuring the samples. Hypogonadism might be more refined and not constantly apparent by low testosterone degrees. For instance, males with primary testicular damage usually have regular testosterone degrees yet high LH. This could be taken into consideration a subclinical or made up kind of hypogonadism. The clinical effects of a separated altitude of LH is not clear yet, however possibly, these males might end up being hypogonadal in the future.

• **Benefits and risks of testosterone replacement therapy in hypogonadal males**

For all hypogonadal males, replacement of testosterone is suggested other than in patients where fertility is preferred (Table 2) or when there are contraindications (Table 3). Induction of fertility in hypogonadotrophic hypogonadism will be discussed later. The biochemical objective of testosterone treatment is to raise ordinary serum testosterone degrees (over days for transdermals and implants or weeks for injectables) into the mid-normal variety (e.g., 400 - 700 ng/dl) for male hypogonadism. Studies have shown that testosterone may have a threshold effect on some criteria such as sexual function yet there seems a dose-related reaction to testosterone therapy for muscular tissue mass, fat mass and

hemoglobin and hematocrit^[11]. A recent research study revealed that testosterone raises muscular tissue mass but aromatization to estradiol is necessary for reduction in fat mass and renovation in sexual function^[12]. **Finkelstein JS** suggested that estradiol in males will certainly be needed for these functions. This elevates some problem about an enhancing trend amongst some practitioners of integrating testosterone replacement treatment with aromatase inhibitors.

Table 2. Benefits and potential risks of testosterone replacement therapy.

Benefits	Potential risks
Maintains secondary sexual characteristics	Acne, oily skin
Improves libido and erectile dysfunction	Gynecomastia
Increases lean/muscle mass and strength	Weight gain/fluid retention at initiation of treatment
Decreases weight, body fat and visceral obesity	Lipids (decrease in HDL)
Increases bone mass	Prostate (benign prostatic hyperplasia and prostate cancer)
Improves energy and vitality	Increased hemoglobin, hematocrit and red cell count
Improves mood and depression	Sleep apnea
Coronary vasodilatation, reduces cardiovascular disease risk	Increased cardiovascular adverse effects

Table 3. Contraindications to testosterone replacement therapy.

Absolute contraindications
Prostate cancer
Male breast cancer
Uncontrolled or poorly controlled congestive heart failure
Untreated lower urinary obstructive symptoms
Erythrocytosis

Absolute contraindications
Severe untreated obstructive sleep apnea

Benefits of testosterone therapy in hypogonadal males

In pre-pubertal hypogonadal boys, testosterone replacement treatment will initiate puberty and generate development of secondary sexual characteristics. Androgen therapy for delayed puberty allows extra timely secondary sexual growth and attends to several of the associated psychosocial issues^[13]. The beginning dosage of testosterone in pre-pubertal children is typically less than the adult dosage such that the boys go through puberty gradually. As a number of the children have constitutional delayed puberty, after the induction to complete puberty, testosterone therapy should be taken out and ideal testing for hypothalamic, pituitary or testicular disorder initiated where long-term testosterone replacement is shown (Table 2).

Testosterone replacement treatment boosts sexual function (libido and erectile function) when testosterone levels are restored to the regular array in more youthful hypogonadal males^[16]. There is conflicting details concerning the ability of testosterone to improve impotence independent of the effects on sex drive^[16]. In older men, lasting research studies on patient reported results are needed to more review the impacts of testosterone replacement treatment on erectile function^[14].

Testosterone replacement therapy boosts bone mineral density in hypogonadal younger and older men^[15]. Meta-analysis researches have also shown testosterone substitute therapy raises bone mineral thickness and reduces rate of bone loss^[16]. Testosterone treatment has not been accepted by the FDA for therapy of osteoporosis as there are no well-controlled data showing that testosterone substitute therapy reduces fracture rate.

Common adverse effects of testosterone replacement in hypogonadal males

Usual adverse occasions of testosterone replacement treatment include advancement of acne and boosted oiliness of skin due to the androgenic effects on sebaceous gland. Plants of acne are normally associated with greater product levels of testosterone and are less common if fairly stable serum testosterone levels are preserved in the mid-adult male array. Gynecomastia may occur with the management of testosterone because of its conversion to estradiol. If

the gynecomastia is serious the dosage might be decreased or an aromatase prevention can be utilized concomitantly with testosterone replacement therapy (Table 2).

The most typical negative impact of testosterone replacement therapy is boost in hemoglobin, hematocrit and red cell indices^[18]. Testosterone replacement therapy boosts hematocrit in anemic hypogonadal guys in a dosage dependent way^[17]. The stimulation of hematopoiesis is affected by age and seems more obvious in older men^[19]. Altitude of hematocrit over the reference variety could lead to increased blood viscosity, which might enhance thrombotic difficulties such as stroke, myocardial infarction, deep vein thrombosis and pulmonary embolism. It is suggested that hypogonadal men with standard hematocrit values over 50% go through a workup prior to testosterone replacement therapy due to the fact that these men may have an increased chance of developing hematocrit degrees above 54%^[18]. Testosterone substitute treatment ought to be kept or phlebotomy executed if the hematocrit is > 54%, waiting until the hematocrit go back to listed below 50%; subsequently testosterone substitute treatment ought to be reinitiated at a minimized dose^[18].

• Surgery

Surgical treatment stays the mainstay of varicocele repair and can be performed via a number of surgical methods: (I) open through retroperitoneal, inguinal, or subinguinal approaches; (II) microsurgically through an inguinal or subinguinal incision; (III) laparoscopically utilizing or single-port sites^[19]; (IV) robotically, using either a transperitoneal method or a subinguinal incision.

Varicolectomy involves ligation of the aberrantly dilated veins within the spermatic cord while maintaining arterial and lymphatic supply and the deferential veins. The site of vein ligation depends upon the approach used. As an example, if varicolectomy is done using an inguinal or subinguinal incision the cremasteric and internal spermatic capillaries are ligated, whereas if it is performed retroperitoneally the testicular vein is ligated. The open and laparoscopic retroperitoneal techniques may include intentional division of the testicular artery over the inner inguinal ring, counting on collateral arterial inflow to supply blood supply to the testis. However, in the inguinal and subinguinal strategies, all ran into arteries are managed^[20].

A big 2009 meta-analysis sustains microsurgical varicolectomy as the gold standard for varicocele

repair, with the lowest rate of hydrocele development (0.4%) and the lowest rate of recurrence (1%) compared with various other methods [21]. A more recent comparison of just randomized controlled tests contrasting microsurgical varicocelectomy to open and laparoscopic varicocelectomy performed for infertility verified these outcomes. 2 of the 4 researches contrasted all 3 medical techniques (open, laparoscopic, and microsurgical) whereas the remaining 2 studies compared open and microsurgical repair work just. The research study located a statistically considerable difference in the reduction of hydrocele development and recurrence in microsurgery compared to laparoscopic and open surgical treatment, with no statistically considerable difference in hydrocele or reoccurrence for laparoscopic versus open surgery [22].

Two small studies demonstrated little distinction in outcomes between subinguinal versus inguinal microsurgical varicocelectomies, however revealed conflicting outcomes concerning postoperative discomfort.

Shiraishiet al. kept in mind boosted scrotal pain with a subinguinal laceration [23]. while Pan et al. associated increased discomfort discovered in the inguinal group in their study to department of muscle mass and fascia [23]. No studies have compared robot transperitonealvaricocelectomy to laparoscopic varicocelectomy, and just one record in 2 patients shows its use in the literature. However, several small research studies have examined using robot-assisted microsurgical varicocelectomies. Shu et al. performed the pilot research contrasting personnel time in microsurgical subinguinalvaricocelectomy with robotic subinguinalvaricocelectomy, and discovered no difference [24].

It is unclear what the indicators were for varicocelectomy, and whether operative time took into account configuration time for the daVinci robotic system. Semen parameters were not measured. A more recent non-randomized, non-controlled study of 154 patients (chronic orchialgia in 106 pts, consisting of some with oligospermia, and oligo- or azospermia in 77 pts) discovered that 77% of the patients with oligospermia and 18% of patients with azospermia had improvement in semen parameters [24].

CONCLUSION

Male hypogonadism is identified by the presence of symptoms or signs of male hypogonadism and consistent serum testosterone levels that are below the

normally accepted adult male range. Once the medical diagnosis is confirmed, the primary goal of treatment is testosterone substitution to accomplish serum testosterone levels that remain in the mid-adult range and the symptoms and signs of hypogonadism are eliminated. Recent developments led to numerous delivery systems for testosterone. For patients with primary hypogonadism testosterone therapy is the approach of choice. For patients with secondary hypogonadism that prefer fertility, replacement with subcutaneous injection of gonadotropins, hCG or human recombinant FSH can be applied to induce testosterone generation by the testis and spermatogenesis. Currently, vasectomy reversal is most commonly done microsurgically, although it has been performed without the help of the microscope. The patient needs to be completely informed about expected benefits and side-effects of the treatment option. The option of the preparation should be a joint decision by a notified patient and the doctor.

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