

Age-Related Changes in Sex Hormone Levels in Men Over 60: The Role of SHBG And Metabolic Factors

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Abstract

Aging in men is naturally accompanied by changes in endocrine regulation, the most significant of which is a progressive decline in androgenic function. According to epidemiological studies, men over 60 years of age experience an annual decrease in testosterone levels averaging 0.8–1.0%, and this physiological process can be significantly exacerbated by obesity and metabolic syndrome.

Keywords: Age-related hypogonadism; Testosterone; Sex hormone-binding globulin (SHBG); Metabolic syndrome; Type 2 diabetes mellitus; Aging; Biomarkers

Introduction

Aging in men is naturally accompanied by changes in endocrine regulation, the most significant of which is a progressive decline in androgenic function [1,5]. According to epidemiological studies, men over 60 years of age experience an annual decrease in testosterone levels averaging 0.8–1.0%, and this physiological process can be significantly exacerbated by obesity and metabolic syndrome [1,8]. The prevalence of biochemical hypogonadism in the 60–69 age group reaches 20%, and among men over 80 years of age exceeds 40% [6,13]. Clinically, this condition manifests as reduced muscle mass and strength, decreased bone mineral density, erectile dysfunction, diminished libido, cognitive impairment, and metabolic disorders, which substantially impair quality of life and increase overall mortality [5,7]. These systemic effects are explained by the pleiotropic action of testosterone, which is involved not only in the regulation of reproductive function but also in maintaining insulin sensitivity, and exerts neuroprotective effects by preventing neuronal death and oxidative stress in the brain [5,19].

Despite the obvious clinical significance of the problem, the diagnosis of age-related androgen deficiency remains challenging [9,12]. The main difficulty is that with age, not only testosterone production changes, but also its transport system in the blood

[3,4]. A key component of this system is sex hormone-binding globulin (SHBG), the concentration of which naturally increases in older men [2,15]. This creates a paradoxical situation: total testosterone levels may remain within normal ranges, while biologically active free testosterone is already substantially reduced [3,9]. An additional complexity is introduced by the close relationship between androgenic status and metabolic disorders [1,11]. Obesity, insulin resistance, and type 2 diabetes mellitus not only frequently accompany aging but are also independent factors that exacerbate testosterone decline [1,18]. The literature discusses the concept of a vicious cycle in which progressive testosterone deficiency worsens existing metabolic disturbances, which in turn further suppress androgenic function [13-17].

Changes in the Hypothalamic-Pituitary-Gonadal Axis with Aging

Age-related involution of the male reproductive system is characterized by complex changes at all levels of the hypothalamic-pituitary-gonadal axis [3,13]. Unlike women, in whom menopause is associated with an abrupt cessation of ovarian function, in men the decline in androgenic function develops gradually, beginning in the fourth to fifth decade of life and progressing with age [3,11]. At the hypothalamic level, there is a disruption in the secretion of gonadotropin-releasing

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hormone, leading to an altered ratio of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) [1,14]. At the pituitary level, gonadotrope sensitivity to GnRH decreases, and the bioactivity of secreted gonadotropins is altered [3,13]. However, the most significant changes occur at the gonadal level: the number of Leydig cells in the testes decreases, along with their functional activity and sensitivity to LH stimulation [3,14]. A number of studies report an age-related increase in LH and FSH levels, indicating that declining testosterone levels no longer adequately suppress gonadotropin secretion [3,13]. Some studies have shown that in men over 70 years of age, the following annual changes are observed: a decrease in total testosterone by 2.6%, dihydrotestosterone by 2.6%, free testosterone by 2.8%, and estrone by 3.2%, with a concurrent increase in SHBG by 1.3%, LH by 1.9%, and FSH by 1.8% per year [3]. Of particular note is the fact that free testosterone declines annually even more markedly than total testosterone, which is explained by the combined effect of reduced testosterone production and increased SHBG levels [3,11]. It is important to note that the decline in testosterone levels is not the only change [3,15]. With age, testosterone metabolism also changes: its conversion to dihydrotestosterone by 5α -reductase and to estradiol by aromatase is enhanced, altering the androgen-to-estrogen ratio in target tissues [13,18].

Physiological Role of SHBG and Age-Related Dynamics

Sex hormone-binding globulin is a glycoprotein synthesized primarily in the liver [2,13]. The main function of SHBG is the transport and regulation of the bioavailability of sex steroids—testosterone, dihydrotestosterone, and estradiol [13,15]. Approximately 98% of circulating testosterone is bound to SHBG and albumin, with only 1–2% present in the free, biologically active form [9,13]. Only free testosterone is able to penetrate cell membranes and interact with androgen receptors [13,18]. SHBG synthesis is regulated by a complex set of factors [2,15]. Estrogens stimulate SHBG production, while androgens and insulin have the opposite effect [2,13]. With age, a physiological increase in SHBG levels is observed, which is associated with several mechanisms [3,15]. First, the androgen-to-estrogen ratio in the blood decreases, shifting the balance toward stimulation of SHBG synthesis [13,15]. Second, age-related changes in liver function, although not critical, may affect protein synthesis, including SHBG [11]. Third, insulin resistance and metabolic status strongly influence SHBG levels [2,15]. Hyperinsulinemia, characteristic of metabolic syndrome, suppresses SHBG synthesis in the liver, leading to a decrease in total testosterone levels [2,15]. Many authors emphasize that for men over 60 years of age, calculation of free testosterone is an essential component of the diagnostic algorithm [9,13]. Ignoring this parameter leads to overdiagnosis of hypogonadism in patients with low SHBG (e.g.,

in obesity) and, conversely, to underdiagnosis in patients with high SHBG [9,15]. Genetic predisposition plays a limited role in age-related testosterone decline, whereas non-genetic factors, including comorbid conditions, are considerably more important [11]. It is important to emphasize that in obese patients, weight loss can lead to restoration of testosterone levels without additional hormone therapy [14,18]. Weight loss significantly increases testosterone levels in men with obesity-associated hypogonadotropic hypogonadism [14,17].

Metabolic Disorders as Modulators of Androgenic Status

The relationship between obesity, type 2 diabetes mellitus, and testosterone decline is one of the most extensively studied in modern endocrinology [1,18]. Numerous studies demonstrate an inverse relationship between body mass index, waist circumference, and levels of both total and free testosterone [1,10]. The mechanisms mediating this relationship are diverse [2,21]. Adipose tissue is an active endocrine organ producing pro-inflammatory cytokines (interleukin-6, tumor necrosis factor- α), which suppress steroidogenesis in Leydig cells [1,12,18]. In addition, adipose tissue expresses aromatase, an enzyme that converts testosterone to estradiol, thereby reducing androgen levels while simultaneously increasing estrogen levels [2,13]. Hyperinsulinemia, characteristic of metabolic syndrome, suppresses SHBG synthesis in the liver, leading to decreased total testosterone levels, whereas free testosterone levels may remain normal or decrease depending on the severity of obesity [2,15]. The clinical significance of this relationship is confirmed by data from the European Male Aging Study (EMAS): in men with confirmed late-onset hypogonadism (total testosterone < 8 nmol/L), the risk of metabolic syndrome is increased 10-fold compared with men with normal hormonal status [8,11].

Conclusion

Age-related changes in androgenic status in men over 60 years of age represent a complex and heterogeneous process determined by the complex interaction of several groups of factors [3,12]. On the one hand, the natural involution of the hypothalamic-pituitary-gonadal axis leads to a progressive decline in testosterone production and an increase in SHBG levels [3,15]. On the other hand, metabolic disorders frequently associated with aging modulate this process, creating individual patterns of hormonal changes [1,10]. In clinical practice, the management of patients with age-related hypogonadism should be based on a differentiated approach [9,14]. In men with obesity and insulin resistance, lifestyle modification should be a priority, as weight loss can lead to restoration of testosterone levels [14,17]. In patients with normal metabolic status and confirmed testosterone

deficiency, testosterone replacement therapy may be considered, the decision for which should be made taking into account individual risks [9,18]. Thus, age-related hypogonadism should be viewed not as an isolated endocrine disorder but as a systemic process integrating age-related, metabolic, and epigenetic factors [8,18]. Further research should focus on establishing normative values for free testosterone in different age groups, developing predictive models that take into account multiple risk factors, and evaluating the long-term outcomes of differentiated therapeutic strategies [9].

References

1. Tylinka M, Broncel M. The relationship between testosterone deficiency and metabolic syndrome in obese men. *Pol Merkuri Lekarski*. 2013; 34: 24-28.
2. La Vignera S, Calogero AE, D'Agata R, Di Mauro M, Tumino S, Condorelli R, et al. Testosterone therapy improves the clinical response to conventional treatment for male patients with metabolic syndrome associated to late onset hypogonadism. *Minerva Endocrinol*. 2008; 33: 159-167.
3. Hsu B, Cumming RG, Naganathan V, Hirani V, Blyth FM, Naganathan V, et al. Temporal trend in androgen status and androgen-sensitive outcomes in older men. *J Clin Endocrinol Metab*. 2016; 101: 1836-1846.
4. Ogoniak L, Sandmann S, Varghese J, Ziller MJ, Neuhau N, Busch AS. Role of genetics in the age-related testosterone decline in men: a UK Biobank study. *Eur J Endocrinol*. 2025; 193: 197-203.
5. Pintana H, Chattipakorn N, Chattipakorn S. Testosterone deficiency, insulin-resistant obesity and cognitive function. *Metab Brain Dis*. 2015; 30: 853-876.
6. Wu FC, Tajar A, Beynon JM, Pye SR, Silman AJ, Finn JD, et al. Identification of late-onset hypogonadism in middle-aged and elderly men. *N Engl J Med*. 2010; 363: 123-135.
7. Yeap BB, Marriott RJ, Antonio L, Dwivedi G, Adams RJ, Ballantyne CM, et al. Associations of testosterone and related hormones with all-cause and cardiovascular mortality and incident cardiovascular disease in men: individual participant data meta-analyses. *Ann Intern Med*. 2024; 177: 768-781.
8. Tajar A, Huhtaniemi IT, O'Neill TW, Finn JD, Pye SR, Lee DM, et al. Characteristics of androgen deficiency in late-onset hypogonadism: results from the European male aging study (EMAS). *J Clin Endocrinol Metab*. 2012; 97: 1508-1516.
9. Bhasin S, Brito JP, Cunningham GR, Hayes FJ, Hodis HN, Matsumoto AM, et al. Testosterone therapy in men with hypogonadism: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2018; 103: 1715-1744.
10. Zhang Z, Chen Y, Li N, Huang C, Lin D, Wang C, et al. Gonadal hormones and metabolic syndrome in middle-aged and elderly males: results from a prospective cohort study in China. *Front Endocrinol (Lausanne)*. 2024; 15: 1365283.
11. Wu FC, Tajar A, Pye SR, Silman AJ, Finn JD, O'Neill TW, et al. Hypothalamic-pituitary-testicular axis disruptions in older men are differentially linked to age and modifiable risk factors: the European male aging study. *J Clin Endocrinol Metab*. 2008; 93: 2737-2745.
12. Tharakan T, Miah S, Jayasena C, Minhas S. Investigating the basis of sexual dysfunction during late-onset hypogonadism. *F1000Res*. 2019.
13. Kaufman JM, Vermeulen A. The decline of androgen levels in elderly men and its clinical and therapeutic implications. *Endocr Rev*. 2005; 26: 833-876.
14. Corona G, Rastrelli G, Monami M, Saad F, Luconi M, Lucchese M, et al. Body weight loss reverts obesity-associated hypogonadotropic hypogonadism: a systematic review and meta-analysis. *Eur J Endocrinol*. 2013; 168: 829-843.
15. Chubb SAP, Hyde Z, Almeida OP, Flicker L, Norman PE, Jamrozik K, et al. Lower sex hormone-binding globulin is more strongly associated with metabolic syndrome than lower total testosterone in older men: the health in men study. *Eur J Endocrinol*. 2008; 158: 785-792.
16. Zhang J, Huang X, Liao M, Gao Y, Tan A, Yang X, et al. Both total testosterone and sex hormone-binding globulin are independent risk factors for metabolic syndrome: results from Fangchenggang area male health and examination survey in China. *Diabetes Metab Res Rev*. 2013; 29: 374-382.
17. Elagizi A, Kohler TS, Lavie CJ. Testosterone and cardiovascular health. *Mayo Clin Proc*. 2018; 93: 83-100.
18. Hsu B, Cumming RG, Naganathan V, Blyth FM, Le Couteur DG, Seibel MJ, et al. Associations between circulating reproductive hormones and SHBG and prevalent and incident metabolic syndrome in community-dwelling older men: the concord health and ageing in men project. *J Clin Endocrinol Metab*. 2014; 99: E2686-E2691.
19. Herman WA, Krzoska A, Pawliczak E, Roszak M, Lacka K. Evaluation of relationships between plasma androgens level and clinical signs of hypogonadism according to age and comorbidity of metabolic syndrome in men. *Pol Merkuri Lekarski*. 2014; 36: 16-21.