HYPOGONADISM IN METABOLIC SYNDROME PATIENTS

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Abstract

Introduction. *Previous studies have shown a high prevalence of low levels of the endogenous sexual hormones in patients with metabolic syndrome (MetS). The aim of this study was to analyze the prevalence of hypogonadism in MetS patients.* ***Materials and Methods.*** *We analyzed the relationship between testosterone levels and components of metabolic syndrome in 381 patients. These patients were divided into two groups: group A – patients with metabolic syndrome (MetS) and hypogonadism (MetS+T) and group B – patients with metabolic syndrome without hypogonadism (MetS-T). Overweight was defined as BMI 26-29.9kg/m^2. Obesity was defined as BMI≥30 kg/m^2. Male hypogonadism or androgen deficiency has been defined as a maximum level of total testosterone up to 3 ng/ml.* ***Results.*** *There were no significant age differences between groups (59.8±8.38 versus 58.31±7.47 years p=0.06). Prevalence of hypogonadism in metabolic syndrome patients was 33.5% (n=128). There were no significant differences between groups in terms of body weight, waist circumference, hip circumference, BMI and blood pressure between groups (all p>0.05). Patients with hypogonadism had significantly higher levels of triglycerides, FPI, HOMA-IR (all p<0.05) and smaller HDL-cholesterol and SHBG (all p<0.05). There was a significant decline in testosterone concentration with increase in age and BMI. 88.3% of the diabetic patients (n=113) had hypogonadism (p=0.0001). Hypogonadism was present in 25% patients (n=32) with 3 components of MetS, 43.8% (n=56) patients with 4 componets of MetS and in 31.2% (n=40) patients with 5 components of MetS (p=0.0001).* ***Conclusions.*** *Hypogonadism is a common occurrence in subjects with MetS. Males with MetS with or without diabetes have lower serum testosterone. Patients with MetS should be investigated for clinical and biochemical signs of hypogonadism and patients with hypogonadism should be investigated for signs of metabolic syndrome.*

keywords*: insulinresistance, hypogonadism, diabetes*

Introduction

The metabolic syndrome (MetS) is a cluster of cardiovascular risk factors: diabetes and raised fasting plasma glucose, abdominal obesity, high cholesterol and high blood pressure. Prevalence of MetS in the general population is estimated to be around 20-25% and increases with age; there is higher incidence in the male population [1,2].

Testosterone (C19H28O2) (T), the main testicular hormone, is a 19-carbonic steroid substance with - OH group in position 17. Testosterone is synthesized from cholesterol in smooth endoplasmatic reticulum of Leydig cells of testes and also in adrenal cortex, liver, kidneys, in fat and muscle tissue, even though in smaller extent - around 5% is daily produced [3]. The normal daily production of testosterone for a healthy man is approximately 4-9 mg (13.9-31.2 nmol/l).

The mechanisms by which T production is decreased as BMI increases are not fully understood, but several facts are known that might be pertinent. Obesity is associated with decreased SHBG production, which increases total testosterone. Obesity is also associated with increased inflammatory cytokine production, as well as increased aromatization of testosteron to estradiole in peripheral fat tissue. Both of these factors then decrease the pituitary production of gonadotropins, which, in turn, decrease testicular production of testosterone [4,5].

Previous studies have shown a high prevalence of low endogenous sex hormones with MetS [6]. With this study we aim to analyze the prelavence of hypogonadism in MetS patients.

Materials and methods

The population studied - The study population was recruited from patients screened for prostate cancer in ”Optimization of the precocious diagnosis of prostate adenocarcinoma at patients with metabolic syndrome by correlating the genetic factors, anatomic-pathological and biochemical” research project, acronym ADENODIAG. The study was held in three medical centers in Bucharest (two urology clinics and a diabetes and metabolic diseases clinic). ADENODIAG had a study population of 414 patients. 33 of these patients (7.97%) were diagnosed with prostate cancer and were excluded from the present study for not having completed all immunological and genetic analysis. The curent study analyzed the relationship between testosterone level and components of MetS in the remaining 381 patients. MetS was diagnosed according to IDF criteria: central obesity – (waist circumference over 94cm in men or BMI over 30kg/m^2) plus any two of the following factors: 1. triglycerides (TG)≥1.695mmol/l (150mg/dl) or treatment; 2. lower high density lipoprotein-cholesterol (HDL-C)<40mg/dl or treatment; 3. blood pressure ≥130/85mmHg or medication; 4. fasting blood glucose≥5.6mmol/l (100mg/dl) or medication for diabetes.

Exclusion criteria were: treatment with testosterone, 5-alpha reductase inhibitors in the last six months (dudasterida, finasteride), infectious diseases of the prostate, the presence of a malignancy other than prostate cancer as well as simultaeous participation in other studies.

These patients were divided into two groups: group A – patients with metabolic syndrome (MetS) and hypogonadism

(MetS+T) and group B – patients with metabolic syndrome without hypogonadism (MetS-T).

Overweight criteria was defined as BMI 26-29.9kg/m^2. Obesity was defined as BMI ≥30kg/m^2.

The diagnosis of benign prostatic hyperplasia was based on prostatic volume (PV) by TRUS (all patients with PV over 30cm^3 were considered with BPH); the prostatic size can also be estimated by DRE, but it tends to underestimate the true prostate size as opposed to TRUS.

Male hypogonadism or androgen deficiency has been defined by some researchers as a total testosterone levels of 2.5 standard deviations below the average in young adults or under 319ng/dl (11 nmol/l) [7]. Clinical criteria of hypogonadism are more ambiguous. Most researchers will agree that levels of total testosterone under 3ng/ml will be defined as symptoms and clinical consequences of hypogonadism.

Clinical examination

Clinical examination included the following parameters: height (cm), weight (kg), waist circumference (WC) (cm) (measured at the midpoint between the lower rib margin and the iliac crest), hip circumference (HC) (cm) (measured as the maximal circumference at femoral trohanters), blood pressure (mmHg), systolic and diastolic, measured in one arm, after ten minutes rest.

Body mass index (BMI) was calculated (body weight in kilograms divided by the square of height in meters) and categorized based on national guidelines as follows: less than 25kg/m^2 (normal), 25–29.9kg/m^2 (overweight), 30–34.9kg/m^2 (obesity class 1), 35-39.9kg/m^2 (obesity class II), >40kg/m^2 (obesity class III).

Digital rectal exams were performed in all patients in order to assess the size of the prostate gland, its consistency, the presence of a node, the mobility of the prostate on palpation, the symmetry of the two lobes, noting the characteristics of any asymmetries, palpation of the seminal vesicle.

Laboratory assays

Fasting blood samples were drawn between 7:00 a.m. and 10:00 a.m. Biochemical analyses including fasting plasma glucose (FPG), HbA1c, total cholesterol (TC), triglycerides (TG), high-density lipoprotein – cholesterol (HDL-C), fasting plasma insulin (FPI), total testosteron (TT), sex hormone binding globulin (SHBG) and prostate-specific antigen (PSA) were performed.

IR (insulin resistance) was determined using Homeostasis Model Assessment (HOMA-IR) (fasting insulin level (mUI/l) x fasting glucose level (mg/dl)/405; a HOMA-IR index value of more than 2.0 was considered as criteria for insulin resistence. The prostate gland volume was measured using transrectal ultrasounds.

Statistical analysis

Data was analyzed using SPSS 16 computer software, and $p<0.05$ was considered to be statistically significant. The normality of variable distribution was determined using both the Kolmogorov-Smirnov and Shapiro-Wilk test. Statistical analysis was performed using one-way analysis of variance to compare means and proportions, respectively Chi square and

Fisher exact tests used to test differences in proportions.

Results

We included 381 patients with MetS, means age 58.8±7.8 years (min 45, max 83). Group A included patients with hypogonadism, n=128 and group B included patients without hypogonadism, n=71. Body weight, WC, HC, BMI, BP do not differ into the two groups (all $p>0.05$). Patients with hypogonadism have triglycerides, FPI, HOMA-IR significantly higher (all $p<0.05$) and smaller HDL-cholesterol and SHBG (all $p<0.05$).

Testosterone concentration had a significant decline with the increase in age. Testosterone levels analyzed in age groups 45-50, 50-59, 60-69, 70-79, and over 80 years were 3.8±0.8ng/ml, 3.7±1.3ng/ml, 3.7±1.4ng/ml, 3.06±0.8ng/ml, respectively 2.7±0.4ng/ml (p=0.03 by ANOVA) (**Figure 1**).

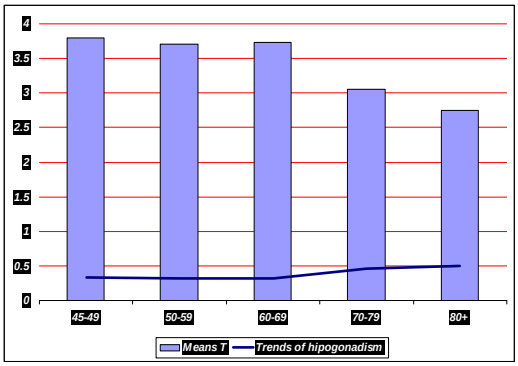

Fig. 1. Means of testostosterone and hypogonadism trend and age groups

MetS and prevalence of hypogonadism

Prevalence of hypogonadism for the entire group was 33.5% (n=128), 35.2% (n=109) in BPH patients and 26.8% (n=19) in patients without prostatic diseases (p=0.21).

In patients with BMI over 30 kg/m^2 63.5% (n=81) of the patients have hypogonadism (p=0.506).

Testosterone levels in overweight, obesity class I, obesity class II and obesity class III were 3.76±1.3ng/ml, 3.75±1.2ng/ml, 2.74±0.6ng/ml respectively 2.57±0.39ng/ml (p=0.03 by ANOVA) (**Figure 2**).

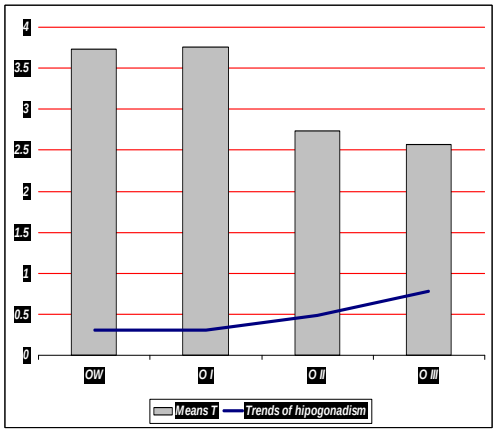

Fig. 2. Means of testostosterone and hypogonadism trend and BMI groups

There was no difference in patients with hypertension between those with or without hypogonadism (p=0.43); hypogonadism was present in 34.4% (n=43) in nonhypertensive patients and in 65.6% patients with hypertension.

In patient with hypertriglyceridemia, hypogonadism was present in 76.8% (n=96) as opposed to only 23.3% (n=29) of the patients with normal level of triglycerides (p=0.01).

In the hypoHDL-cholesterol group 116 patients (45.3%) had hypogonadism (p=0.12). Of the diabetic patients, 88.3% (n=113) had hypogonadism (p=0.0001).

Hypogonadism was present in 25% patients (n=32) with 3 components of MetS, 43.8% (n=56) patients with 4 components of MetS and in 31.2% (n=40) patients with 5 components of MetS (p=0.0001) (**Figure 3**).

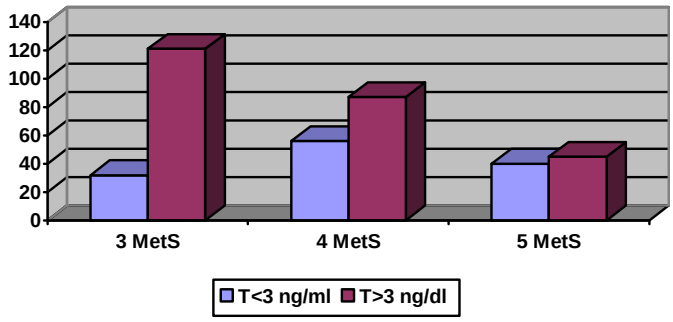

Fig. 3. Prevalence of hypogonadism and components of MetS

Testosterone level and anthropometric and clinical parameters

There were negative correlation coefficients between testosterone levels and weight, BMI, WC and older age that are statistically significant, but correlations are not very strong (**Table 1**).

Table 1. Pearson's correlation between testosterone and clinical and anthropometric parameters

	Testosterone	Age	Weight	BMI	WC	HC	SBP	DBP
Testosterone	1	-0.140**	-0.133**	-0.298**	-0.144**	-0.096	-0.028	-0.058
Age	-0.140**	1	-0.281**	-0.027	-0.192**	-0.164**	0.118*	0.077
Weight	-0.133**	-0.281**	1	0.827**	0.727**	0.616**	0.114*	0.096
BMI	-0.298**	-0.027	0.827**	1	0.669**	0.556**	0.182**	0.158**
WC	-0.144**	-0.192**	0.727**	0.669**	1	0.826**	0.180**	0.151**
HC	-0.096	-0.164**	0.616**	0.556**	0.826**	1	0.186**	0.139**
SBP	-0.028	0.118*	0.114*	0.182**	0.180**	0.186**	1	0.550**
DBP	-0.058	0.077	0.096	0.158**	0.151**	0.139**	0.550**	1

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).

The equation that described the decline in testosterone concentration with an increase in age and BMI in non diabetic men was: Testosterone=12.61-(0.34*age)-(0.212*BMI) where testosterone is in ng/ml, age is in years, and BMI is weight in kilograms divided by the square of height in meters (r^2=0.244).

In diabetic men, the equation was Testosterone=6.625-(0.021*age)-(0.059*BMI) (r^2=0.35).

In non diabetic patients 24.4% of variation of testosterone is explained by BMI and age and is highly significant at p<0.0001. In diabetic male, 35% of variation of testosterone is explained by BMI and age and is highly significant at p<0.0001.

The regression model only describes the relationship between testosterone, age, and BMI in MetS patients; the model could not be used to predict normal population sample, which would include normal weight. However the model could be used to predict normal values for MetS patients.

There was a positive correlation between testosterone levels and HDL-cholesterol and negative correlations with triglycerides, cholesterol, fasting plasma insulin, fasting plasma glucose and HOMA-IR that were

statistically significant, but these correlations are not very strong (**Table 2**).

Table 2. Pearson's correlation between testosterone and biochemical parameters

	Testosterone	BMI	TG	HDL-C	Chol	FPG	FPI	HbA1c	HOMA-IR
Testosterone	1	-.298**	-.148**	.138**	-.117*	-.162**	-.140**	-0.041	-.169**
BMI	-.298**	1	.135**	-.180**	.103*	0.022	.189**	0.075	.143**
TG	-.148**	.135**	1	-.356**	.424**	.298**	.312**	.238**	.310**
HDL-C	.138**	-.180**	-.356**	1	-0.018	-.182**	-.213**	-.206**	-.232**
Chol	-.117*	.103*	.424**	-0.018	1	.110*	0.038	.166**	0.055
FPG	-.162**	0.022	.298**	-.182**	.110*	1	.199**	.548**	.523**
FPI	-.140**	.189**	.312**	-.213**	0.038	.199**	1	.102*	.889**
HbA1c	-0.041	0.075	.238**	-.206**	.166**	.548**	.102*	1	.261**
HOMA-IR	-.169**	.143**	.310**	-.232**	0.055	.523**	.889**	.261**	1

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).

Means of testosterone in MetS patients

Means of testosterone were smaller in patients with BMI over 30kg/m2, with hypertension, with hypertrigliceridemia (TG over 150mg/dl), with hypoHDL-cholesterolemia (HDL-cholesterol under 40mg/dl) and diabetes, but there was a statistical significance observed only for BMI and diabetes (0.029 respectively 0.02) (**Table 3**).

Table 3. Means of testosterone and MetS

		Testosterone ng/ml		
		Means (SD)	p value	Eta^2
Obesity	Yes	3.6 (1.24)	0.029	0.03
	No	3.74 (1.36)		
Hypertension	Yes	3.6 (1.3)	0.348	0.002
	NO	3.7 (1.16)		
Hypertriglyceridemia	Yes	3.57 (1.27)	0.063	0.009
	NO	3.83 (1.32)		
HipoHDL-cholesterolemia	Yes	3.77 (1.31)	0.133	0.006
	No	3.57 (1.29)		
Diabetes	Yes	3.55 (1.28)	0.006	0.02
	No	3.99 (1.3)		
Metabolic syndrome	3 components	3.88 (1.14)	0.005	0.028
	4 components	3.6 (1.5)		
	5 components	3.32 (1.09)		

Discussions

Prevalence of hypogonadism in MetS patients was 33.5%. The results were concordant with the results found in Males (HIM) study [8], which used a definition for hypogonadism of total testosterone concentration <300ng/dl (10.41nmol/l) and obtained a crude prevalence rate of 38.7% in men aged ≥45 years [8].

In the Massachusetts Male Ageing Study, the prevalence of androgen deficiency varies between 6.0% and 12.3% where hypogonadism was defined as a total testosterone level <200ng/dl (6.94nmol/l), or

at least three symptoms of hypogonadism with a total testosterone level between 200 and 400ng/dl (13.88nmol/l) [9].

This study showed that men with three or more components of MetS had lower levels of testosterone. This is in line with the findings of Kaplan et al. who found an inverse relationship between the number of components of MetS and the total testosterone levels, even in non-diabetic men [10].

Visceral obesity is a central element of the MetS. Recent clinical studies have also confirmed that total testosterone is inversely associated with body mass index, waist-hip ratio and percentage of body fat [11,12,13,14]. Visceral obesity is strongly related to MetS and insulin resistance, and has a negative correlation to testosteron levels [15].

In our study, BMI and age predict 35% of variability of testosteron in diabetic patients as opposed to 24.4% in nondiabetic men. There was a significant decline in testosterone concentration with increase in age and BMI.

Hypertension has also been associated with hypogonadism, as well as its long known affiliation with cardiovascular risks. Mulligan et al. have shown that more men with hypertension have low testosterone levels [16]. Smith et al. showed that androgen deprivation in men with prostate cancer could also induce hypertension and arterial stiffness, even within a span of only several months [17].

Diabetes is commonly associated with low testosterone levels. Among men with diabetes, the prevalence of hypogonadism has been reported to range from 20% to 64% [18,19,20]. In a meta-analysis, Ding et al. found approximately 20 studies that showed a high prevalence of hypogonadism in diabetic men [21]. The relationship was so strong in four of these studies that it was stated that low testosterone levels predicted future diabetes. Although abdominal visceral fat is an important mediator of this relationship, testosterone may have additional direct effects on insulin resistance. In our study, 88.3% of diabetic patients had hypogonadism. An American study on patients with type 2 diabetes determined that the overall prevalence of hypogonadism was 25% with free testosterone <5.0ng/dl (0.174nmol/l) and 44% with total testosterone <300ng/dl [22]. In addition, the HIM study reported a greater prevalence of diabetes among hypogonadal men (30.9%) than eugonadal men (17.9%) [8]. Higher prevalence in our study can be explained by the fact that patients were recruited from hospital and therefore had a more serious associated pathology than the general population.

In several of these studies, testosterone was positively associated with insulin sensitivity (or inversely associated with insulin resistance) [23,24,25,26], but other studies were not able to demonstrate a significant correlation [27]. In our study, we found a correlation between testosterone and HOMA IR, but it was weak in that respect.

Prospective epidemiological studies cannot proove direction of causation, as reverse causation from unrecognized confounders are already present at baseline and cannot be excluded. Low testosterone levels could either contribute to or be a very early consequence of the mechanisms finally leading to the development of diabetes. The data supports the existence of a bidirectional relationship between testosterone and insulin resistance.

Conclusions

In conclusion, 33.5% of MetS patients aged over 45 have subnormal testosterone concentrations. Hypogonadism was common in subjects with MetS. Males with MetS with or without diabetes have lower serum testosterone. Patients with MetS should be investigated for clinical and biochemical signs of hypogonadism and patients with hypogonadism should be investigated for signs of MetS. Testosterone level should be measured in these populations.

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REFERENCES

1. **www.idf.org/metabolic_syndrome**, website of the International Diabetes Federation.

2. **AlSaraj F, McDermott JH, Cawood T, McAteer S, Ali M, Tormey W, Cockburn BN, *et al*. Prevalence of the metabolic syndrome in patients diabetes mellitus.** Ir J Med Sc **178**(3)**:** 309-313, 2009.

3. **Bidlingmaier F, Dörr HG, Eisenmenger W, Kuhnle U, Knorr D.** Contribution of the adrenal gland to the production of androstenedione and testosterone during the first two years of life. *J Clin Endocrinol Metab* 62(2): 331-5, 1986.

4. **Laaksonen DE, Niskanen L, Punnonen K, Nyyssonen K, Tuomainen TP, Salonen R, Rauramaa R, Salonen JT.** Sex hormones, inflammation and the metabolic syndrome: a population-based study. *Eur J Endocrinol* 149: 601-608, 2003.

5. **Kalyani RR, Dobs AS.** Androgen deficiency, diabetes and the metabolic syndrome in men. *Curr Opin Endocrinol Diabetes Obesity* 14: 226 –234, 2007.

6. **Muller M, Grobbee DE, den Tonkelaar I, Lamberts SW, van der Schouw YT.** Endogenous sex hormones and metabolic syndrome in aging men. *J Clin Endocrinol Metab* 90: 2618-2623, 2005.

7. **Vermeulen A.** Androgen replacement therapy in the aging male–a critical evaluation. *J Clin Endocrinol Metab* 86:2380–2390, 2001.

8. **Mulligan T, Frick MF, Zuraw QC, Stemhagen A, McWhirter C.** Prevalence of hypogonadism in males aged at least 45 years: the HIM study. *Int J Clin Pract* 60: 762-9, 2006.

9. **Araujo AB, O'Donnell AB, Brambilla DJ et al.** Prevalence and incidence of androgen deficiency in middle-aged and older men: estimates from the Massachusetts Male Aging Study. *J Clin Endocrinol Metab* 89: 5920-6, 2004.

10. **Kaplan SA, Meehan AG, Shah A.** The age related decrease in testosterone is significantly exacerbated in obese men with the metabolic syndrome. What are the implications for the relatively high incidence of erectile dysfunction observed in these men? *J Urol* 176: 1524-1528, 2006.

11. **Pitteloud N, Mootha VK, Dwyer AA et al.** Relationship between testosterone levels, insulin sensitivity, and mitochondrial function in men. *Diabetes Care* 28: 1636-42, 2005.

12. **Kalme T, Seppala M, Qiao Q et al.** Sex hormone-binding globulin and insulin-like growth factor-binding protein-1 as indicators of metabolic syndrome, cardiovascular risk and mortality in elderly men. *J Clin Endocrinol Metab* 90: 1550-6, 2005.

13. **Smith MR, Lee H, Nathan DM.** Insulin sensitivity during combined androgen blockade for prostate cancer. *J Clin Endocrinol Metab* 91: 1305-8, 2006.

14. **Fukui M, Kitagawa Y, Nakamura N et al.** Association between serum testosterone concentration and carotid atherosclerosis in men with type 2 diabetes. *Diabetes Care* 26: 1869-73, 2003.

15. **Seidell JC, Bjomtorp P, Sjostrom L, Kvist H, Sannerstedet R.** Visceral fat accumulation in men is positively associated with insulin, glucose and C-

peptide levels, but negatively with testosterone levels. *Metabolism* 39: 897-901, 1990.

16. Mulligan T, Frick MF, Zuraw QC, Stemhagen A, McWhirter C. Prevalence of hypogonadism in males aged at least 45 years: the HIM study. *Int J Clin Pract* 60: 762-769, 2006.

17. Smith MR, Lee H, Nathan DM. Insulin sensitivity during combined androgen blockade for prostate cancer. *J Clin Endocrinol Metab* 91: 1305-1308, 2006.

18. Dhindsa S, Prabhakar S, Sethi M, Bandyopadhyay A, Chaudhuri A, Dandona P. Frequent occurrence of hypogonadotropic hypogonadism in type 2 diabetes. *J Clin Endocrinol Metab* 89: 5462-8, 2004.

19. Mulligan T, Frick MF, Zuraw QC, Stemhagen A, McWhirter C. Prevalence of hypogonadism in males aged at least 45 years: the HIM study. *Int J Clin Pract* 60: 762-9, 2006.

20. Corrales JJ, Burgo RM, Garca-Berrocal B et al. Partial androgen deficiency in aging type 2 diabetic men and its relationship to glycemic control. *Metabolism* 53: 666-72, 2004.

21. Ding EL, Song Y, Malik VS, Liu S. Sex differences of endogenous sex hormones and risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA* 295: 1288-1299, 2006.

22. Dhindsa S, Prabhakar S, Sethi M, Bandyopadhyay A, Chaudhuri A, Dandona P. Frequent occurrence of hypogonadotropic hypogonadism in type 2 diabetes. *J Clin Endocrinol Metab* 89: 5462-8, 2004.

23. Basaria S, Muller DC, Carducci MA, Egan J, Dobs AS. Hyperglycemia and insulin resistance in men with prostate carcinoma who receive androgen-deprivation therapy. *Cancer* 106: 581-8, 2006.

24. Pitteloud N, Mootha VK, Dwyer AA et al. Relationship between testosterone levels, insulin sensitivity and mitochondrial function in men. *Diabetes Care* 28: 1636-42, 2005.

25. Smith MR, Lee H, Nathan DM. Insulin sensitivity during combined androgen blockade for prostate cancer. *J Clin Endocrinol Metab* 91: 1305-8, 2006.

26. Kalme T, Seppala M, Qiao Q et al. Sex hormone-binding globulin and insulin-like growth factor-binding protein-1 as indicators of metabolic syndrome, cardiovascular risk and mortality in elderly men. *J Clin Endocrinol Metab* 90: 1550-6, 2005.

27. Corrales JJ, Burgo RM, Garca-Berrocal B et al. Partial androgen deficiency in aging type 2 diabetic men and its relationship to glycemic control. *Metabolism* 53: 666-72, 2004.

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