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ORIGINAL ARTICLE

ERECTILE DYSFUNCTION AND TOTAL TESTOSTERONE LEVEL IN MEN AGED 35-45

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Abstract. Objective: *To find the association between erectile dysfunction and testosterone level in men aged 35-45 years.* ***Materials and Methods:*** *We selected men aged 35 to 45 with/without erectile dysfunction, and compared the total testosterone level in both groups. Altogether 93 men were included for evaluation, 73 men with and 20 without erectile dysfunction. Each man filled out the International Erectile Function Index questionnaire and was measured for testosterone level and the sex hormone binding globulin three times every 45 days for 3 months.* ***Results:*** *We found significant differences between the studied patients and those of the control group in the questionnaire score and the total testosterone level. We did not register fluctuations in the blood flow of the arteria profunda penis bilaterally in all men.* ***Conclusions:*** *Our study shows that partial deficiency of total testosterone in some men aged 35 to 45 may also be a possible prerequisite for the occurrence of erectile dysfunction.*

Key words: *testosterone, erectile dysfunction, men*

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INTRODUCTION

As men age, erectile dysfunction (ED) is an increasingly common complaint, with a prevalence of 70% in patients aged 70 years and older. In these patients, it is due to concomitant cardiovascular or metabolic diseases and to some medications used to treat them [1]. Other possible causes include psychiatric disorders [2] or psychogenically related erectile dysfunction [3, 4].

Androgens are known to be necessary for an adequate erectile response. Some authors have observed in their studies that men with low androgen levels have a significant reduction in frequency, amplitude, and penile rigidity [5]. However, the level of total testosterone (TT) at which ED occurs is controversial. In addition, castration usually causes a decrease in sexual function, which normalizes after treatment with exogenous androgens [6].

Erectile dysfunction occurs not only in adults but also in young men. In their study, Huang IS et al. reported a low serum TT level and ED in 10% of men under 40 years of age [1]. Some studies have found that

20% to 40% of men with ED have low free testosterone levels [7], but others have failed to confirm these findings [2]. The decrease in serum TT level in the young men is multifactorial and is most often associated with overweight and obesity [8, 9].

Zitzmann et al. (2006) in their study of men aged 50 to 85 years found a loss of libido at serum TT values of 12-15 nmol/L and the onset of ED at serum TT values below 8 nmol/L [10]. However, the threshold level of serum TT below which ED occurs in young men remains unknown at present.

AIM OF THE STUDY

To find the association between ED and serum TT level in men aged 35-45, in an attempt to determine whether there is a clear discrimination threshold below which it becomes clinically significant.

MATERIALS AND METHODS

Study site, design, and population

From the electronic database of Sveta Sofia Hospital, we selected 1521 Bulgarian men aged 35 to 45 years with ED and different body mass index (BMI) examined in the andrology office for the period from January 2013 to December 2019. We also randomly selected a control group of 20 clinically healthy men with a normal BMI of the same age without ED who visited the andrological office for a prophylactic examination.

Institutional Review Board Statement

All clinical, laboratory, and ultrasound parameters for the study group of men were extracted from our electronic database. The participants in this study were dully informed and signed a written consent form to participate in it with the explicit condition to remain anonymous. The project was reviewed and approved by the Independent Ethics Committee (IEC) of the Hospital in Obstetrics and Gynecology „Sv. Sofia“ in accordance with the Declaration of Helsinki: IEC code No. 3/28.11.2022, for studies involving humans.

Interview

In our study, we used the International Erectile Function Index (IEFI) [11]. All 93 participants in the study declared having partners. For this reason, we did not include the statement “I am not currently having sex” in the questionnaire.

Clinical and laboratory evaluation

BMI was determined for each participant [12]. We tested each patient’s serum TT level and the sex hormone binding globulin (SHBG) three times every 45 days for a period of 3 months. Furthermore, we performed blood collection after a mandatory 30-minute rest period between 8.00 a.m. and 9.00 a.m. Hormonal analysis was performed with a Mini Vidas apparatus from Bio-Mérieux Company, and standard reagents were added according to the enzyme-linked fluorescence assay method. To calculate the value of free testosterone, we used the free androgen index (FAI) formula:

FAI = (100xT)/SHBG

Ultrasonographic technique

Ultrasound scan of the penis in all men was also performed with a Mindray NS2 device with a 7.5 MHz sector converter for surface organs after the third blood collection for serum TT level. The analysis of the blood flow of the deep penile artery (DPA) included: peak systolic velocity (PSV), end diastolic velocity (EDV) and resistive index (RI) [13].

Data analysis

The age, BMI, TT, SHBG, FAI, IEFI result, diameter of DPA, PSV, EDV and RI values in all patients were entered into the IBM SPSS Statistics (ver. 25) software. The critical significance level used was $p \leq 0.05$.

Distribution of men according to clinical and laboratory results

According to clinical and laboratory results, the selected group of men (n=73) was divided into 5 groups according to BMI and the average values of the three samples for TT as follows:

1. Healthy control group, men without ED, normal BMI, TT >19.04 nmol/l (n=20)
2. Second group, men with ED, normal BMI, TT < 14.28 nmol/l (n=18);
3. Third, fourth and fifth groups, respectively: men with ED, overweight and TT < 14.28 nmol/l, (n=27); men with ED, obesity first degree and TT < 14.28 nmol/l, (n=16), men with ED, obesity second degree and TT < 14.28 nmol/l, (n=12).

RESULTS

Demographic. clinical and laboratory characteristics

The demographic, clinical, laboratory and ultrasound parameters have also been thoroughly presented by us [14, 15] and the correlation dependencies are summarized in Table 1.

Table 1. Correlation Dependencies

	IEFI	BMI	TT	FAI
IEFI	1.000			
BMI	.393**	1.000		
TT	-.529**	-.634**	1.000	
FAI	-.392**	-.155**	.469**	1000

Legend: (p< 0.05*, p< 0.001**) IEFI – IEFI result, BMI – body mass index, TT – total testosterone, FAI – free androgen index

A comparison between the values obtained for the average serum TT level and the IEFI result is presented in Fig. 1.

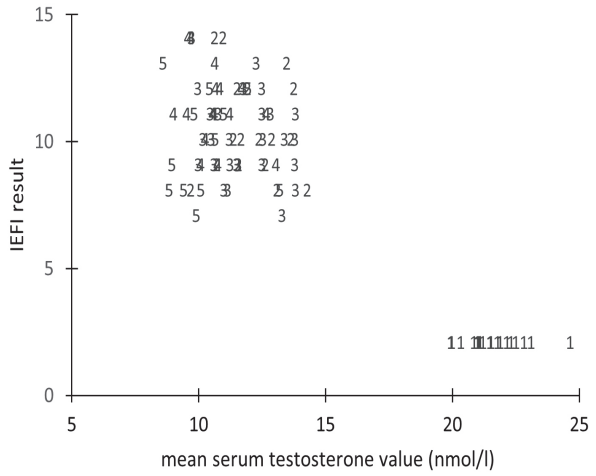

Fig. 1. Scatter plot comparing the mean values of TT for all subjects and the number of points part of the questionnaire. The number of the group to which each subject was assigned was used as a marker

DISCUSSION

Of the 1,521 men surveyed, 618 met the age criteria of 35 to 45 years. Persons with classical primary or secondary hypogonadism (n=21) were excluded from this study. To stratify the cohort regarding ED, only men living within a partnership were included. This led to exclusion of men living alone (n=37). Persons with ED and sexually transmitted infection (n=176), with cardiac diseases (n=17), diabetics (n=86), with congenital anomalies (n=7) and with Peyronie's disease (n=6) were excluded after appropriate assessment of clinical examination and the microbiology diagnostics of seminal fluid and urine. We also excluded men with proven psychogenic ED from our study after evaluation by a psychiatrist (n=268).

Altogether 73 men aged between 35 and 45 years were included for evaluation and data collection was comprehensive for our pilot study. This was communicated to us through the IEFI questions.

Most authors still associate the onset of ED in men aged 35-45 years with serum TT values below normal [1, 5, 6]. According to the guidelines, defined for clinical practice by the Endocrine Society, the normal serum TT level for men should be between 10.4-34.7 nmol/L [16, 17]. The recommendations of the International Society of Andrology, the International Society for the Study of Aging Men, the European Association of Urology and the American Society of Andrology, define a minimum serum TT level of 7.98 nmol/L. Our study demonstrates that the points from IEFI questions significantly increased ($p<0.001$) at serum TT level <14.28 nmol/l compared to the points from IEFI questions of the control group and serum TT level > 19.04 nmol/l. This observation of our results shows that ED in young men occurs not when TT values are below normal, but even below the average values of the normal range. So far, we have not come across a similar study in the available literature to be able to compare these observations to ours. These observations suggest that further studies with more participants are needed to determine whether there is a clear discriminatory threshold of serum TT level below which ED becomes more prevalent in men aged 35-45.

Zitzmann et al. (2006) in their study of men aged 50 to 85 years found a loss of libido at serum TT values of 12-15 nmol/L and the onset of ED at serum TT values below 8 nmol/L [10]. In our study, we observed the onset of ED without loss of libido at a serum TT level of 8.64-14.28 nmol/L. This result indicates that there is a significant difference in the serum TT level at which ED occurs between the young and the older men, which is another argument to recommend additional androgen studies in young men with ED in the future.

According to Swerdloff et al., it is necessary to confirm low serum TT concentrations in men with a baseline value in the mildly hypogonadal range, because on repeated measurement, 30% of these patients show a normal level [18]. Following these recommendations, we examined TT in our group of patients three times over a three-month period, which we believe reflected a correct/representative value.

No significant difference in the mean values of the serum TT was found between the second, third, fourth and fifth groups, but we observed a clear trend of a gradual decrease in its level with increasing BMI. A European study on aging in men found that 73% of those with reduced androgen levels were overweight or obese [19]. Of interest however is ED in the men of the second group with a normal BMI. It is possible that the serum TT level, alone or in combination with other factors, except for an elevated BMI, is a prerequisite for ED. These observations and the moderate correlation we found between IEFI questions and BMI ($r =0.393^{**}$, $p<0.001$) suggest that an increased BMI is less important for the occurrence of ED in young men than a serum TT level < 14.28 nmol/L for prolonged period ($r = -.0529^{**}$, $p<0.001$)

Some researchers have found that 20% to 40% of men with ED have low levels of free testosterone [7]. We found a moderately negative correlation between FAI and the IEFI questions ($r = -0.392^{**}$, $p<0.001$), which suggests a lower importance of free testosterone for ED in this group of patients.

Various parameters, such as the DPA, PSV, EDV, and RI, degree of arterial dilation, and acceleration time, have been proposed to diagnose arteriogenic ED. But PSV is the most accurate indicator of arterial disease [13, 20]. Color Doppler ultrasound was performed after the third serum TT blood collection to ensure that for three months the men had a serum TT level below 14.28 nmol/L for a prolonged period. The average diameter of the DPA and blood flow parameters in our study were close to those of Jung et al. (2018) [13]. The lack of significant differences in blood flow parameters between the individual groups, thereby rejects the vascular factor as a cause for ED in our study.

Limitations

1. The serum TT level was monitored only three times over three months and that does not allow us to tell how ED would develop in the future if it remained for a longer period < 14=28 nmol/L
2. The number of examined patients included in this pilot study is relatively small and we are considering expanding it.

CONCLUSIONS

Our study shows that partial deficiency of total testosterone in some men aged 35 to 45 may also be a possible prerequisite for the occurrence of erectile dysfunction.

Data Availability: *The data used to support the findings of this study are available from the author upon request.*

Funding: *This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.*

Conflicts of Interest Statement: *The author declares no conflict of interest.*

Informed Consent from Participants: *The participants in this study were fully informed and signed a written consent to participate in it with the explicit condition to remain anonymous.*

Ethical statement: *The project was reviewed and approved by the independent ethics committee (IEC) of the Hospital in Obstetrics and Gynecology „Sv. Sofia“ in accordance with the Declaration of Helsinki: IEC code No. 3/ 28.11.2022, for studies involving humans.*

REFERENCES

1. Huang IS, Mazur DJ, Kahn BE, et al. Risk factors for hypogonadism in young men with erectile dysfunction. J Ch Med Ass. 2019; 82: 477-481. doi: 10.1097/JCMA.0000000000000099.
2. Selvin E, Burnett A, Platz E. Prevalence and risk factors for erectile dysfunction in the US. Am J Med, 2007; 120(2): 151-157.
3. Capogrosso P, Colicchia, M, Ventimiglia E, et al. One patient out of four with newly diagnosed erectile dysfunction is a young man-worrisome picture from the everyday clinical practice. J Sex Med. 2013; 10: 1833-1841. doi: 10.1111/jsm.12179.
4. Rastrelli G, Maggi M. Erectile dysfunction in fit and healthy young men: psychological or pathological? Transl Androl Urol. 2017; 6: 79-90. doi: 10.21037/tau.2016.09.06.
5. Mulhall JP, Trost LW, Brannigan RE, et al. Evaluation and Management of Testosterone Deficiency: AUA Guideline. J Urol. 2018; 200: 423-32. doi: 10.1016/j.juro.2018.03.115.
6. Santos HO, Howell S, Teixeira FJ. Beyond tribulus (Tribulus terrestris L.): The effects of phytotherapics on testosterone, sperm, and prostate parameters. J Ethnopharmacol. 2019; 235: 392-405. doi: 10.1016/j.jep.
7. Buvat J, Lemaire A. Endocrine screening in 1022 men with erectile dysfunction: clinical significance and cost-effective strategy. J Urol. 1997; 158: 1764–1767. doi: 10.1016/s0022-5347(01)64123-5.
8. Pivonello R, Menafra D, Riccio E, et al. Metabolic Disorders and Male Hypogonadotropic Hypogonadism. Front Endocrinol. 2019; 10: article 345. doi.org/10.3389/fendo.2019.00345.
9. Scovell JM, Ramasamy R, Wilken N, et al. Hypogonadal symptoms in young men are associated with a serum total testosterone threshold of 400 ng / dl. BJU Int. 2015; 116: 142-146. doi: 10.1111/bju.12970.
10. Zitzmann M, Faber S, Nieschlag E. Association of Specific Symptoms and Metabolic Risks with Serum Testosterone in Older Men. J Clin Endocrinol Metab 2006; 91(11): 4335–4343.
11. Rosen RC, Riley A, Wagner G, et al. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urol. 1997; 49: 822-830. doi: 10.1016/s0090-4295(97)00238-0
12. Weir CB, Jan A. BMI Classification Percentile and Cut Off Points. 2022 Last Update: June 27.
13. Jung DC, Park SY, Lee JY. Penile Doppler ultrasonography revisited. Ultrasonography. 2018; 37: 16–24. doi: 10.14366/usg.17022.
14. Lazarov G, Mladenov V. Changes in the hypothalamic-pituitary-gonadal axis in men aged 37 to 45 years with a testosterone level below the average values of the standard for a prolonged period. Case Reports and Reviews: Open Access. 2023; 4: 135.
15. Lazarov G. Estradiol/testosterone ratio and erectile dysfunction in men aged 35-45 E2/T ratio and ED in men aged 35-45. Folia Medica. 2025;67(4): 1-5. doi: 10.3897/folmed.67.e143525.
16. Bhasin S, Buckwalter G. Testosterone supplementation in older men: a rational idea whose time has not yet come. J Androl. 2001; 22: 718-731. doi.org/10.1002/j.1939-4640.2001.tb02570.x
17. Harman SM, Metter EJ, Tobin JD, et al. Longitudinal effects of aging on serum total and free testosterone levels in healthy men. Baltimore Longitudinal Study of Aging. J Clin Endocrinol Metab. 2001; 86: 724-731. doi: 10.1210/jcem.86.2.7219.
18. Swerdloff R, Wang C, Cunningham G, et al. Long-term pharmacokinetics of transdermal testodterone gel in hypogonadal men. J Endocrinol Metab, 2000; 85(12): 4500-4510.
19. Poobalan A, Aucott L. Obesity among young adults in developing countries: a systemic overview. Curr Obes Rep, 2016; 5(1): 2-13.
20. Aversa A, Crafa A, Greco EA, et al. The penile duplex ultrasound: How and when to perform it? Andrology. 2021; 9: 1457-1466. doi: 10.1111/andr.13029.