

ORIGINAL RESEARCH—ENDOCRINOLOGY

Testosterone Deficiency in Patients with Erectile Dysfunction: When Should a Higher Cardiovascular Risk Be Considered?

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ABSTRACT

Introduction. Low testosterone levels (low T) increase the cardiovascular (CV) risk of men with erectile dysfunction (ED). T levels associated with a higher CV risk are unknown.

Aim. To determine the prevalence of CV risk factors associated with low T as defined by European Guidelines and their contribution to low T, overall and at different ages.

Methods. Multicenter, cross-sectional, observational study conducted in Spain among men with ED aged ≥ 18 years visiting Urology/Andrology offices for sexual dysfunction. Anthropometric, clinical, and laboratory data, including total T (TT) values, were collected for 1,278 men.

Main Outcome Measures. Risk factors were assessed in men with TT ≤ 8 , 8–12, and ≥ 12 nmol/L, and two-group comparisons were made. Bivariate and multivariate logistic regression analyses were performed to calculate odds ratios for low T after adjusting for possible confounding factors.

Results. Mean age (standard deviation) was 58.0 (9.2) years. Age and prevalence of CV risk factors was similar in men with TT ≤ 8 nmol/L or 8–12 nmol/L and significantly higher than in men with TT > 12 nmol/L. Low T was therefore considered as TT ≤ 12 nmol/L, with a prevalence of 33.3%. Obesity, hypertension, hyperlipidemia, and severe ED were the variables most strongly associated with low T: obesity in middle-aged men; hyperlipidemia, and hypertension in older men. Severe ED was a risk factor in both groups. Hypolipidemic therapy had the greater effect in young men. Multivariate analysis showed that severe ED and obesity were the strongest predictors of low T.

Conclusion. T levels associated with increased CV risk could go as high as 12 nmol/L in men with ED, with distribution of risk factors showing differences according to age. Obesity and severe ED are the best predictors of low T-related CV risk. **Martínez-Jabaloyas JM. Testosterone deficiency in patients with erectile dysfunction: when should a higher cardiovascular risk be considered? J Sex Med 2014;11:2083–2091.**

Key Words. Testosterone; Hypogonadism; Cardiovascular Diseases; Androgen Deficiency; Erectile Dysfunction; Metabolic Syndrome; Diabetes; Hypertension; Hypercholesterolemia; Obesity; Abdominal Obesity; Sexual Dysfunction

Introduction

Erectile dysfunction (ED) is a common disorder in aging men affecting over 50% of men aged 40–70 years [1]. ED is frequently associated with modifiable risk factors such as diabetes, hypertension, hyperlipidemia, obesity, smoking, and a sedentary lifestyle [1–4]. ED has shown to increase the risk for cardiovascular (CV) events and all-cause mortality, showing also a trend to

increase the risk for CV mortality [5]. ED nearly doubles the risk for CV events in men with diabetes [6]. Men with ED are therefore advised to undergo a detailed medical assessment for early intervention on cardiovascular health [7,8].

ED is one of the most common symptoms of testosterone deficiency syndrome (TDS), a condition associated with advancing age that is characterized by low levels of serum testosterone (low T) and the presence of compatible symptoms that are

not specific of the condition [9,10]. The relationship between ED and low T has been recently reviewed [11].

Low T is thought to be associated with diabetes, metabolic syndrome (MetS), and CV disease [12]. A meta-analysis of epidemiological data has shown that MetS is associated with lower levels of total T (TT) [13]. Longitudinal evidence has also shown that low T is associated with a higher risk for developing MetS, although it is unclear which is the cause and which is the consequence [14]. Some authors also support that low T might be a fundamental component of MetS [15].

Association between MetS and low T levels has shown to be more evident in men with ED [13], which may result in increased CV risk in these men. Comorbidities such as diabetes, hypertension, and obesity have been found to be associated with increased CV diseases in men with low T, independently of age [14]. Looking for low T among men with CV comorbidities and, conversely, identifying CV comorbidities when hypogonadism is found, is therefore of great importance [14].

Among symptoms associated with low T, ED is an important reason to seek medical advice. Most guidelines recommend the determination of serum T in men with ED signs [9,10]; however, a biochemical threshold for the definition of low T is still lacking, with differences among professional societies. Determining T thresholds may be of value as a reference to start testosterone replacement therapy (TRT) but also to adopt more intensive measures, beyond lifestyle modifications, to reduce CV risk. European Guidelines recommend TRT in men with ED and low T (defined as TT ≤ 8 nmol/L; 230 ng/dL) and also in those with "borderline" T levels (8–12 nmol/L) and a clinical picture of low T, where a short trial is advisable [9]. However, the T level associated with an increased CV risk in men with ED is unknown.

Aim

We analyzed the prevalence of common CV risk factors in a large cohort of men with ED with the aims of (i) analyzing which TT threshold, using the two thresholds proposed by European guidelines (8 and 12 nmol/L) as a reference, is associated with a higher prevalence of CV risk factors; and (ii) identifying which of these CV risk factors is associated with a higher likelihood for low T. The relative weight of each risk factor across the lifespan was also assessed.

Method

This was a multicenter, cross-sectional, observational study conducted in Spain with the objective of assessing the relationship of ED and cardiovascular risk factors, including the prevalence of low T levels, among men seeking specialized medical attention due to sexual dysfunction. Patients aged ≥ 18 years were consecutively recruited by 394 urologists and andrologists from January to September 2009. Inclusion criteria included a diagnosis of ED according to the Erectile Function domain of the International Index of Erectile Function (IIEF-EF) [16], the ability to answer a self-questionnaire, and to have provided written informed consent. The only exclusion criterion was refusal to participate in the study. An independent Ethics Committee approved the study protocol. All information was centralized in a coordination center.

Data Collection

Data were collected in a single visit and included: age, anthropometric data (body mass index [BMI] and waist circumference [WC]), tobacco use and alcohol consumption, and medical conditions (hyperlipidemia, diabetes, and hypertension). Information about the presence of these comorbidities was self-reported (confirmed by previous prescription of treatment and/or lifestyle changes for their correction) when not available in the clinical records. Diagnosis was based on current local guidelines targets. Hypolipidemic therapy was also recorded given the T-lowering effect of statins [17]. Obesity and abdominal obesity were defined as having a BMI ≥ 30 kg/m² and WC ≥ 102 cm, respectively [18]. Men were considered smokers when smoking for at least 1 year. Moderate alcohol consumption was defined as having up to two glasses of wine or beer per day or 3–4 hard alcohol drinks per week. Excessive intake was considered as any intake exceeding the stated amounts [19]. Severity of ED was assessed using the IIEF-EF, which includes questions 1–5 and 15 of the IIEF [16]. Questions are scored from 1 to 5 points, with ED defined as a total score value ≤ 25 . Severity is classified as follows: mild (22–25), mild-to-moderate (17–21), moderate (11–15), and severe (6–10). A single point plasma TT level measurement was performed between 7 and 11 hours in subjects lacking a TT determination in the last 6 months. Laboratory tests were performed at the reference laboratory of participating centers. Serum TT was measured using a chemiluminiscent

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