Relationship of Testis Size and LH Levels with Incidence of Major Adverse Cardiovascular Events in Older Men with Sexual Dysfunction

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J Sex Med 2013;10:2761–2773

Measurement of testis volume (TV) is a reliable clinical procedure that predicts reproductive fitness. However, the role of TV in overall and cardiovascular (CV) fitness has never been studied.

The aim of this study is to analyze the clinical correlates of TV in patients with sexual dysfunction (SD) and to verify the value of this parameter and its determinants (i.e., luteinizing hormone [LH] levels) in predicting major adverse CV events (MACE).

Materials and Methods

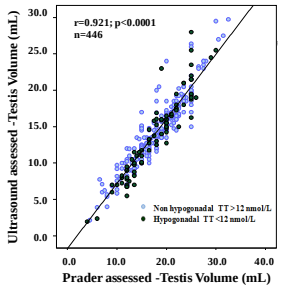
This is an observational prospective cohort study considering a consecutive series of 2,809 subjects without testiculopathy (age 51.2 13.1) consulting for SD was retrospectively studied. A subset of this sample (n = 1,395) was enrolled in a longitudinal study. Several clinical and biochemical parameters were investigated.

Results

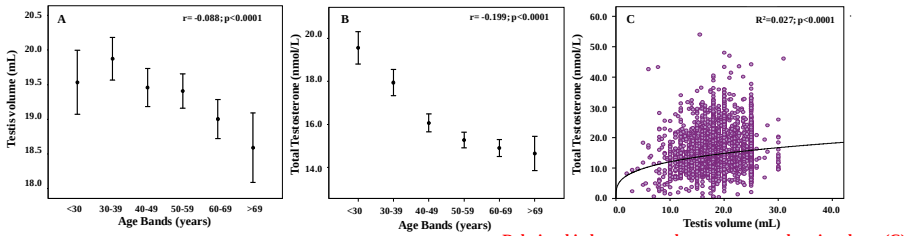
After adjusting for confounders, TV was negatively associated with both LH (Adj. r = -0.234; P < 0.0001) and follicle-stimulating hormone (Adj. r = -0.326; P < 0.0001). In addition, overweight/obesity, smoking, and alcohol abuse increased as a function of TV (hazard ratio [HR] = 1.041 [1.021–1.061], P < 0.0001; 1.024 [1.005–1.044], P = 0.012; 1.063 [1.015–1.112], P = 0.009, respectively). Furthermore, mean blood pressure was positively related to increased TV (Adj. r = 0.157; P < 0.0001). The effect of these lifestyle factors on TV were only partially related to changes in gonadotropin levels. In the longitudinal analysis, after adjusting for confounders, TV was associated with a higher incidence of MACE (HR = 1.066 [1.013–1.122]; P = 0.014), and the stepwise introduction in the Cox model of lifestyle factors, mean blood pressure and body mass index progressively smoothed out the association, which was no longer statistically significant in the fully adjusted model. Conversely, the association of higher LH levels with increased incidence of MACE was not attenuated by the progressive introduction of the aforementioned confounders in the model.

CROSS-SECTIONAL STUDY

Relationship between clinical (Prader orchidometer) and ultrasonographic evaluation of mean testis volume in a subset of patients who consulted for both sexual dysfunction and infertility



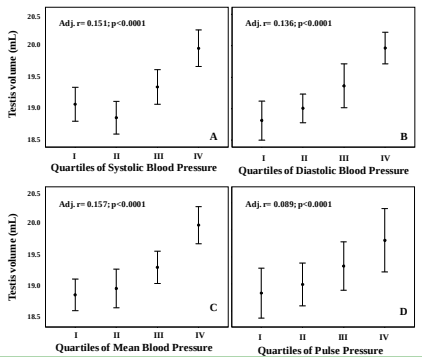
Associations between age and testis volume (A) or total testosterone (B)



Relationship between total testosterone and testis volume (C)

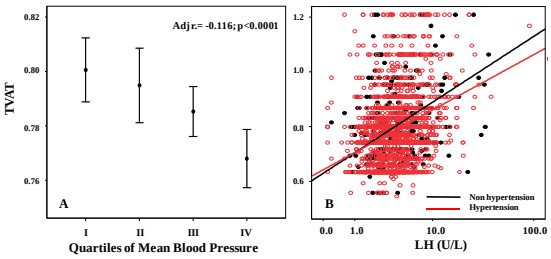
Change in testis volume as a function of quartiles of systolic, diastolic, mean, and pulse pressure

The insets *indicate the age and total testosterone-adjusted data*



Change in testis volume-adjusted testosterone (TVAT) as a function of quartiles of mean blood pressure (A) or luteinizing hormone (LH) levels (log scale [B])

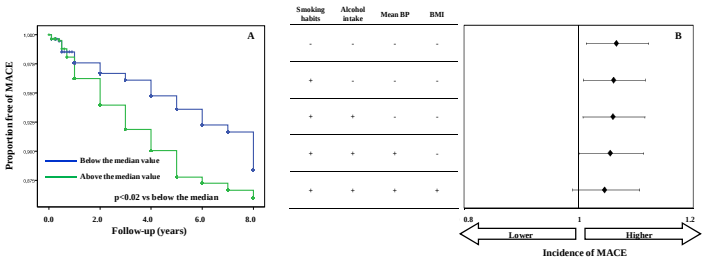
All data have been adjusted for age



LONGITUDINAL STUDY

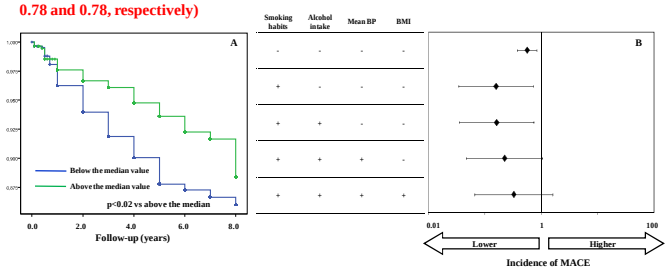
(A) Risk for incident major adverse cardiovascular events (MACE) as derived from Kaplan–Meier curves in subjects with testis volume below and above the median value (testis volume 19.75 mL and 20.00 mL, respectively).

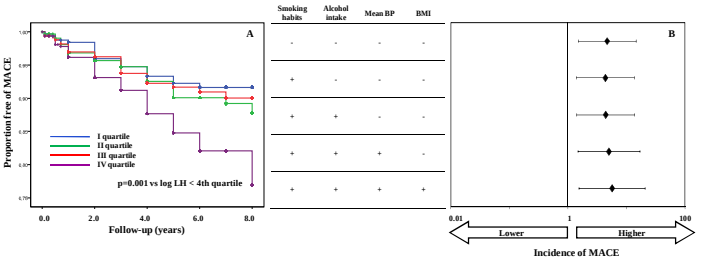
(B) Hazard ratio and 95% confidence interval for MACE as a function of mean testis volume, as derived from different Cox regression models with stepwise introduction of further confounding factors. All the Cox regression models are also adjusted for age, total testosterone levels, and Chronic Disease Score. BP = blood pressure; BMI = body mass index



(A) Risk for incident major adverse cardiovascular events (MACE) as derived from Kaplan–Meier curves in subjects with testis volume-adjusted testosterone (TVAT) below and above the median value (TVAT < 0.78 and 0.78, respectively)

(B) Hazard ratio and 95% confidence interval (log scale) for MACE as a function of TVAT, as derived from different Cox regression models with stepwise introduction of further confounding factors. All the Cox regression models are also adjusted for age and Chronic Disease Score. BP = blood pressure; BMI = body mass index





(A) Risk for incident major adverse cardiovascular events (MACE) as derived from Kaplan–Meier curves according to quartiles of log[LH]

(B) Hazard ratio and 95% confidence interval (log scale) for MACE as a function of log[LH], as derived from different Cox regression models with stepwise introduction of further confounding factors. All the Cox regression models are also adjusted for age, testis volume-adjusted testosterone, follicle-stimulating hormone and Chronic Disease Score.

Conclusions

Our data show that in SD subjects, TV and LH are associated with an adverse CV risk profile that mediate the higher TV-associated incidence of MACE. High LH levels are an independent marker of CV risk. Further studies are needed for clarifying determinants and mechanisms of testis enlargement that, beyond gonadotropins, could mediate the increased incidence of MACE.