Low Plasma Testosterone is Associated with Elevated Cardiovascular Disease Biomarkers

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ABSTRACT
We have studied a panel of relatively new cardiovascular disease (CVD) biomarkers to examine the relationship between T levels and markers of CVD.

Materials & Methods: We performed a retrospective cohort study in a group of 1,534 hypogonadal men from the clinical database of Singulex, Inc. We measured T levels and markers of CVD. CVD participants were defined as patients with a low T level (T < 250 ng/dL). We used logistic regression to analyze the association between T levels and markers of CVD.

Results: T levels decreased linearly with worsening BMI, p-value for trend < 0.0001. For each biomarker, the percent of the patient population that was above the reference limit increased with lower T levels. Hypogonadal men (T < 250 ng/dL) were at increased CVD risk based on blood based biomarkers. Elevated levels of cTnI, IL-6, TNF-α, IL-17A, ET, leptin, and NTproBNP independently predicted low T when adjusted for age and BMI. After adjustment for age and BMI, NTproBNP and Leptin independently predicted low T.

Conclusions: These findings demonstrate a relationship between low T levels and increased CVD risk.

INTRODUCTION

The evidence for a relationship relating low testosterone levels with cardiovascular disease (CVD) has been slowly growing over the past decade. Recent studies investigating this relationship have demonstrated increased circulating levels of CVD biomarkers in hypogonadal men. Additionally, we explore the (for the most part) unknown relationship between sex hormones and traditional biomarkers and whether testosterone levels maintain a relationship with these biomarkers. We hypothesized that decreased levels of sex hormones would result in increased levels of CVD biomarkers. These findings are critical for detecting cardiovascular disease risk, including in those with low T levels. We observed that T levels were inversely related to traditional CVD biomarkers, including CVD. These findings are critical for detecting cardiovascular disease risk, including in those with low T levels.

MATERIALS & METHODS

Subjects

The Singulex Clinical Laboratory (SCL) is a CLIA licensed, CAP accredited clinical laboratory that maintains a database consisting of lab tests ordered on patients that were thought to be at risk for developing CVD or hypertension. In order to determine if biomarkers were increased in hypogonadal men, a retrospective cohort study was performed using SCL laboratory data. In total, 1,534 hypogonadal men were identified. The median T level was 420 (304-565) ng/dL. An inverse relationship between plasma T level and the occurrence of myocardial cell damage, vulnerable plaque, and vascular inflammation. This is the first study to examine the relationships between testosterone and high-sensitivity CVD biomarkers in a cohort of 1,534 hypogonadal men.

Methods

We used logistic regression models. Hypogonadal men were partitioned by BMI groups (<25, 25-29, and >29) then the percent of patients with elevated cTnI, IL-6, TNF-α, IL-17A, ET, leptin, and NTproBNP was determined using an ANOVA linear contrast model. The percent of patients beyond the 99th%-tile RL was determined using a Mann-Whitney U test. The percent of patients that were above the reference limit for each biomarker was determined using a t-test. The percent of patients below the reference limit for T was determined using a one-sample t-test.

Results

T levels decreased linearly with worsening BMI, p-value for trend < 0.0001. For each biomarker, the percent of the patient population that was above the reference limit increased with lower T levels. Hypogonadal men (T < 250 ng/dL) were at increased CVD risk based on blood based biomarkers. Elevated levels of cTnI, IL-6, TNF-α, IL-17A, ET, leptin, and NTproBNP independently predicted low T when adjusted for age and BMI. After adjustment for age and BMI, NTproBNP and Leptin independently predicted low T.

Conclusions

These findings demonstrate a relationship between low T levels and increased CVD risk. Elevated levels of cTnI, IL-6, TNF-α, IL-17A, ET, leptin, and NTproBNP independently predicted low T when adjusted for age and BMI. After adjustment for age and BMI, NTproBNP and Leptin independently predicted low T.

POTENTIALS

Hypogonadal men (defined by low testosterone, T) and increased CVD determined by traditional CVD biomarkers. Patients were partitioned by BMI groups (<25, 25-29, and >29) then the percent of patients with elevated cTnI, IL-6, TNF-α, IL-17A, ET, leptin, and NTproBNP was determined using an ANOVA linear contrast model. The percent of patients beyond the 99th%-tile RL was determined using a Mann-Whitney U test. The percent of patients that were above the reference limit for each biomarker was determined using a t-test. The percent of patients below the reference limit for T was determined using a one-sample t-test.