



Research Article

The Relationship Between Serum Testosterone Level as an Independent Variable in Men with the Risk Factors for Coronary Artery Disease & Rehospitalization for Acute Coronary Syndrome

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Abstract

Background: Despite the numerous studies and medical research that have addressed the relationship between testosterone deficiency & coronary artery disease, most of these studies have overlooked the relationship between testosterone deficiency and the risk factors that contribute to the development of coronary atherosclerosis such as diabetes, hypertension & hyperlipidemia as well as the risk for recurrent hospitalization for acute coronary syndrome. **Aim of the study:** The study's objective is to clarify the relationship between coronary artery disease, rehospitalisation for acute coronary syndrome, concomitant diseases like hyperlipidemia, hypertension & diabetes mellitus in correlation with testosterone deficiency as an independent variable. **Method:** The study was conducted on 167 people over the age of 50 years who presented to the emergency room with acute coronary syndrome whether the first time or recurrent acute coronary syndrome. We looked in those patients at the presence of other diseases that are a risk factors for ischemic heart disease. We measured serum testosterone level upon admission.

Results: There is a strong link between testosterone deficiency and an increased risk of recurrent hospitalization due to acute coronary syndrome and testosterone deficiency has negative impact on the risk factors for ischemic heart disease, which further increases the risk for coronary atherosclerosis.

Introduction

Testosterone is a steroid hormone that belongs to the family of androgens, and it is the primary male sex hormone [1]. Testosterone is produced primarily in the testicles in men, and in smaller amounts in the ovaries in women. Testosterone plays a role in many physiological functions in the body, such as heart health, brain function, and male primary and secondary sexual characteristics [2]. The level of testosterone in adult men ranges between 300 and 1,000 nanograms/dL (ng/dL), but it decreases with age, as testosterone levels decrease by about 1-2% annually after the age of 40 and decrease by 10% to 20% after the age of 50.

Testosterone is also present in women at a rate ranging between 15 and 70 ng/dL, but it decreases by 50% after menopause [3].

Symptoms of testosterone deficiency are weak sexual desire, osteoporosis, and mood changes. There is a strong relationship between testosterone deficiency and heart disease, especially coronary artery disease, as many studies have shown that men who suffer from testosterone deficiency are more susceptible to heart disease [4], Such as coronary artery disease and heart failure [5]. Other studies have shown the relationship between testosterone deficiency and the development of type 2 diabetes, which is a major risk factor for heart disease [5]. Testosterone deficiency

can also lead to development of hypertension [6]. Other studies have linked testosterone deficiency to osteoporosis and cancer [7], however, the relationship between testosterone level and heart disease is complex, and we will address this complex relationship in this study.

Method

167 patients presented to emergency room at King Abdul-Aziz University Hospital with acute coronary syndrome are included in this study.

Inclusion criteria

1. Patients admitted as acute coronary syndrome with positive angiograms for coronary atherosclerosis. Requiring stenting of the coronary arteries, in which they have diabetes mellitus, hypertension and hyperlipidemia.
2. Aged 50 years or older.

Exclusion criteria

1. Patients diagnosed with hypogonadism.
2. Patients on testosterone replacement therapy.
3. Patients admitted with a presumed diagnosis of ACS who had a normal or non-obstructive coronary angiogram and did not require stenting of the coronary arteries.

Demographic analyses were conducted, such as age, gender, comorbidities, social background, smoking history family history of coronary artery diseases, physical examination including heart rate and blood pressure. Blood tests were sent for serum testosterone level, serum glucose level, and lipid profile. The results were analysed statistically through multiple linear regression to study the relationship by using the dependent variable (Y) to represent the presence or absence of coronary artery disease, using the variable (X) to represent the testosterone percentage. The

following multiple linear regression equation is used to model the relationship between variables:

$$Y = \beta_0 + \beta_1 X_1 + \epsilon$$

Where:

Y: dependent variable (blood pressure, blood glucose level & serum cholesterol level)

β_0 : regression constant

β_1 : Regression coefficient for the independent variable X_1 (testosterone percentage)

ϵ : line term

Statistical tests are used to determine whether the relationship between testosterone and coronary artery disease is statistically significant. The results of multiple linear regression analysis can also be used to predict the probability of developing coronary artery disease due to a specific risk factor for ischemic heart disease, through the negative impact of testosterone (independent variable) on the risk factors for ischemic heart disease.

Results

According to (Table 1), it shows the demographic characteristics of the samples in study, where the average age was 58.4 years, with a standard deviation of 7.7 years, while the average weight was 66.8 kg, with a standard deviation of 11.7 kg. The percentage of smokers was 27.7% among the patients, while The percentage of those who stopped smoking was 8.3%, while the percentage of patients with hypertension was 20.3%. The percentage of patients with hyperlipidemia was 7.1%. As for patients with first-time admission with acute coronary syndrome, the percentage was 34.7%, while patients with recurrent admission for acute coronary syndrome the percentage was 11.3%. As for the P-value, they were all less than 0.05, which means that the data is statistically significant.

Demographic Characteristics	All Subjects (n=167)	patients BP (n=21)	first-time admission for ACS(58)	prior admission for ACS(19)	P Value
Age, mean (SD), y	58.4 (7.7)	56.4.1(8.5)	55.7 (9.8)	59.46 (9.8)	<0.001
Weight, mean (SD), kg	66.8 (11.7)	65.6 (10.8)	66.8 (10.6)	68.0 (13.2)	<0.001
Smoking status, no. (%)					
Non-smokers	107 (64%)	4 (19%)	23 (39.6%)	8 (42.1%)	<0.001
Former smokers	14(8.3%)	8 (38%)	5 (8.6%)	4 (21.05%)	<0.001
Current smokers	46 (27.7%)	9 (43%)	16(51.8%)	7 (46.85%)	<0.001
Family history of hypertension, no. (%)	34 (20.3%)	8 (38%)	12 (20.6%)	8 (42.1%)	<0.001
CVD, no. (%)	13 (7.7%)	5 (23.8%)	8 (13.7%)	5 (26.5%)	<0.001
Stroke, no. (%)	12 (7.1%)	3 (14.2%)	4 (6.81%)	3 (15.7%)	<0.001
Cholesterol mean, mmol/L	187.5 (22.05)	188.9 (11.2)	187 (11.15)	186 (12.32)	0.058
T mean (SD), ng/dL	299 (52.2)	284(65.18)	285 (55.8)	284 (58.65)	<0.001

Table 1: Demographic & Clinical Characteristics of all Men in The Study

(Table 2) shows that the regression model explains 10.1% of the variance in the dependent variable ($SS = 37342.32$ / Total $SS = 369188.6$), while 89.9% of the variance is attributed to the “residuals” (Residual $SS = 331846.3$). The F test indicates that the regression model is statistically significant ($F = 6.114073761$, $p\text{-value} = 0.000575277$), meaning there is less than 0.05 probability that the regression model is random, and the R^2 measure indicates that the model is relatively accurate.

	Df	SS	MS	F	Significance F
Regression	3	37342.32	12447.44	6.114073761	0.000575277
Residual	163	331846.3	2035.867		
Total	166	369188.6			

Table 2: Regression and Residual values for the sample in the study.

(Table 3) shows the clinical characteristics of the patients in the study, where the average heart rate reached 102 bpm, with a standard deviation of 5.3, while the average blood pressure measurement reached 140 mmHg, with a standard deviation of 18.5 mmHg for those with hypertension. While for patients with diabetes mellitus, the average blood glucose level was 124.7 mg/dL, with a standard deviation of 11.2

For patients with first time admission due to acute coronary syndrome, the average heart rate was 122.7 bpm, with a standard deviation of 13.6, while the average systolic blood pressure measurement was 128 mm Hg with a standard deviation of 16.5 mm Hg, the average serum testosterone level was 285 ng/dL, with a standard deviation of 62.2 ng/dl. The average blood glucose level was 111 mg/dL, with a standard deviation of 18 mg/dL. The average cholesterol level was 190.1mg/dL with a standard deviation of 19.9mg/dL.

For patients with recurrent admission due to acute coronary syndrome, the average heart rate was 124.7 bpm, with a standard deviation of 12.5, while the average systolic blood pressure measurement was 157 with a standard deviation of 6.25. The average level of serum testosterone was 261 ng/dl, with a standard deviation of 66.5. The average blood glucose level was 146mg/dL with a standard deviation of 19 mg/dL, and the average serum cholesterol level was 189.52 mmol/L with a standard deviation of 20.5 mmol/l.

For STEMI patients, the average heart rate was 122.8 bpm with standard deviation of 12.2 bpm, while the average systolic blood pressure measurement was 139 mm Hg with a standard deviation of 17.24 mm Hg, the average serum testosterone level was 271 ng/dL, with a standard deviation of 58.02, the average blood glucose level was 112mg/dL, with standard deviation of 13.6 mg/dL, while the average serum cholesterol level was 190.78 mmol/L with standard deviation of 20.1 mmol/L.

For NSTEMI patients, the average heart rate was 122.6 bpm, with a standard deviation of 12.5 bpm, while the average systolic blood pressure measurement was 138 mm Hg with a standard deviation of 18.02 mmHg. The serum testosterone level was 288 ng/dL, with a standard deviation of 48.3 ng/dL, the average blood sugar level was 110 mg/dL, with a standard deviation of 3.35 mg/dL, while the average serum cholesterol level was 191.3 mmol/L with a standard deviation of 17.3 mmol/L. As for the P-value, they were all less than 0.05, which means that the data is statistically significant.

Demographic Characteristics	All Subjects (n=167)	patients BP (n=21)	patients DM (n=21)	first-time admission (n=58)	prior admission (n=19)	NSTEMI (n=24)	STEMI (n=34)	P Value
HR mean (SD)	102.7(15.3)	140.7(185.3.54)	105.7(11.23)	122.7(13.5)	124.7(14.6)	122.6(12.5)	122.8(12.2)	<0.001
SPO2%mean (SD)	88.7(7.6)	87.63(5.25)	89.6(6.6)	88.8(5.3)	87.9(8.02)	87.7(8.6)	88.01(5.23)	<0.001
hyperlipidemia(mg/Dl)mean (SD)	187.53(20)	185.77(18.02)	190.44(17.58)	190.1(19.9)	189.52(20.5)	191.33(17.33)	190.78(20.01)	<0.001
Testosterone(ng/dL.)mean (SD)	299 (52.2)	301 (49.2)	299 (6.6)	285 (62.2)	287(66.5)	288(48.3)	285 (58.02)	<0.001
Diabetes(mg/dL)mean (SD)	120(22)	114(23)	140(26)	111(18)	108(19)	110(22)	112(28)	<0.001
Diastolic BP mmHg mean (SD)	56.41(8.5)	58.4.1(6.5)	55.66(7.5)	57.24(6.35)	58(8.8)	57(6.25)	57.8(6.5)	<0.001
Systolic BP mmHg mean (SD)	28.1(4.4)	30(3.3)	28.5(3.87)	28.9(2.88)	301(2 3)	29.8(5.4)	30(4.14)	<0.001

Table 3: The clinical characteristics of the samples in the study

Statistical analysis

(Figure 1) shows the extent of the correlation between testosterone deficiency in relation to coronary artery disease, diabetes mellitus, hypertension & hyperlipidemia. The normal probability plot represents a linear regression, with the F value = 0.0347 and the P-value <0.001, R -VAUE = 0.163. This indicates that the correlation is significant between testosterone deficiency as independent variable for coronary artery disease, diabetes mellitus, hypertension and hyperlipemia.

From our data in this study that looked at the difference between the actual value and the expected values, the average difference did not exceed 4.4, and this is another indication of the extent to which testosterone deficiency is linked to coronary artery disease, diabetes mellitus, Hypertension & hyperlipidemia.

Normal Probability Plot

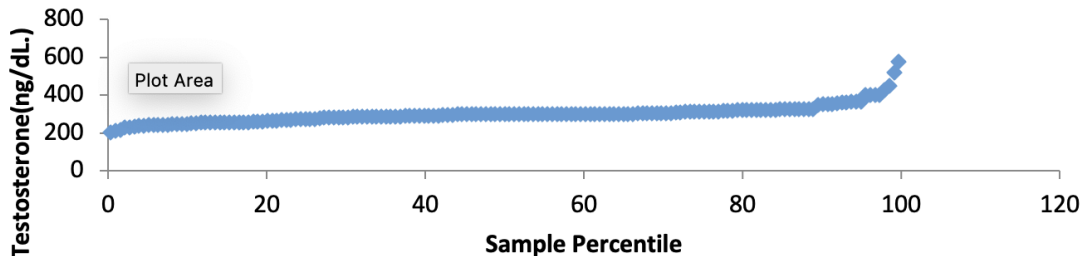


Figure 1: normal probability plot sample vs testosterone(ng/dl)

(Figure 2) shows the extent of the relationship between testosterone deficiency and hyperlipidemia. The scattered curve indicates that all the values are concentrated in one area and that the outliers are very small, which indicates the extent of the significance of the statistical data, as well as the extent to which hyperlipidemia is related to testosterone deficiency.

Hyperlipidemia Line Fit Plot

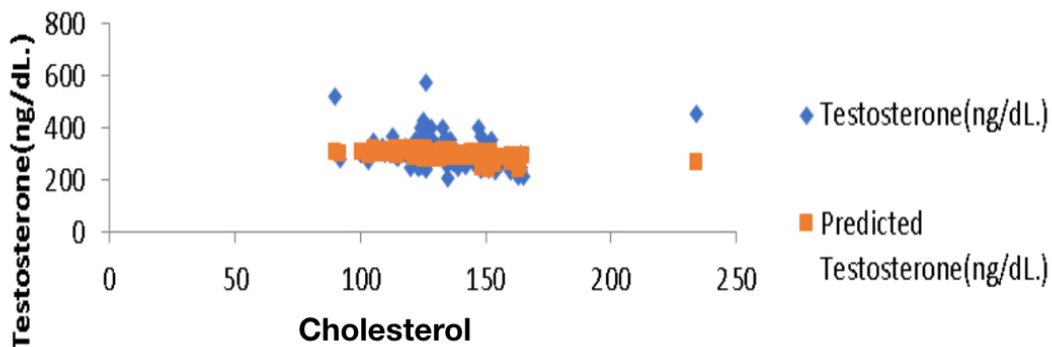


Figure 2: Hyperlipidemia line fit plot vs serum testosterone level

(Figure 3) shows the extent of the relationship between testosterone deficiency and blood pressure. Through the scattering curve, we notice that all the values are concentrated in one area and that the outliers are very small, which indicates the extent of the significance of the statistical data, as well as the extent to which hypertension is related to testosterone deficiency.

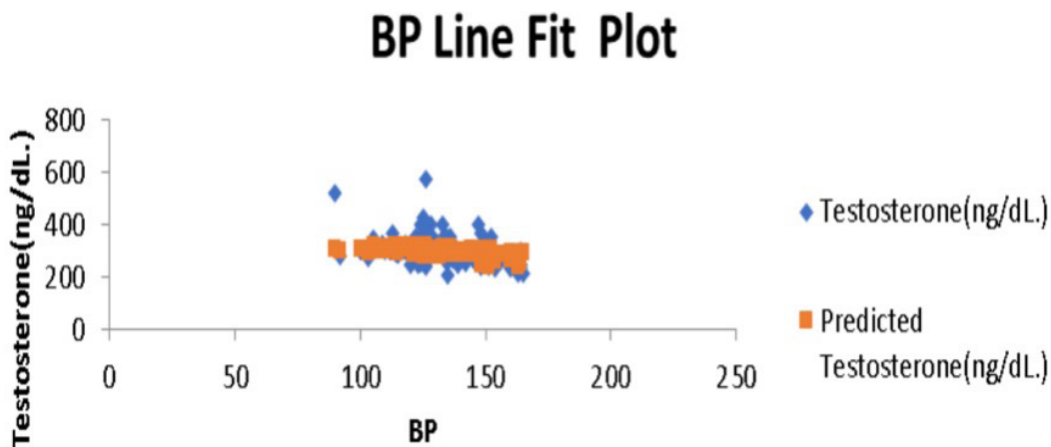


Figure 3: BP line fit plot vs testosterone level

(Figure 4) shows that all values are concentrated in one area and that the extreme values are very small, which indicates the importance of statistical data as well as the extent of the association between testosterone deficiency and diabetes mellitus.

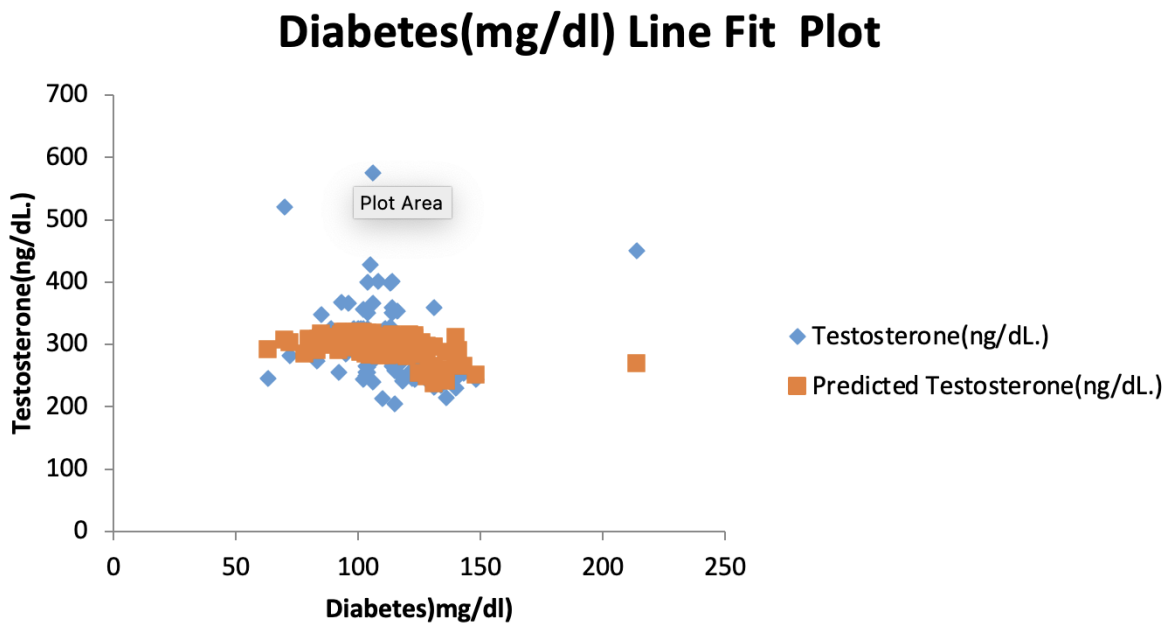


Figure 4: DM line fit plot vs serum testosterone level

(Figure 5) shows the numerical values representing the “residual” (samples). These data represent points in the statistical context model, where residual values provide information about the range and precision of the model estimate. These values indicate that the model or process is relatively accurate. Some outliers indicate a small errors in the model or process.

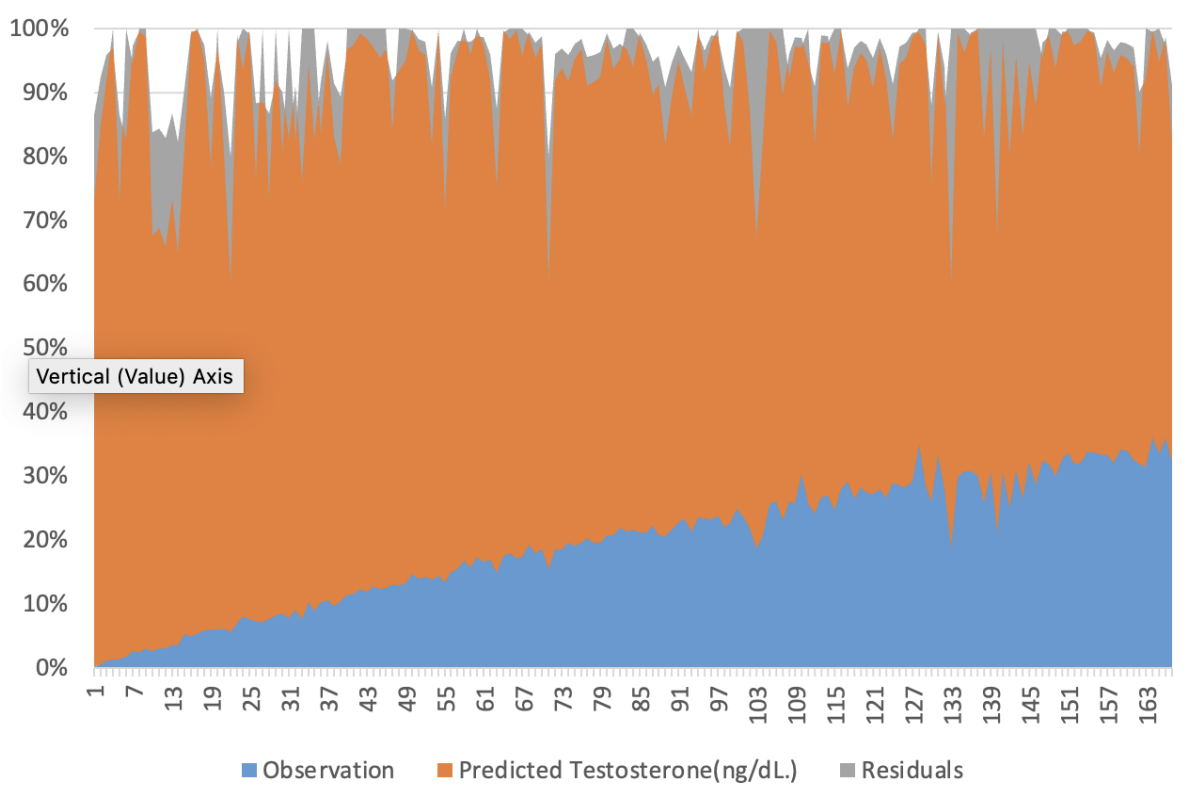


Figure 5: Residual values data in the statistical context model for Hyperlipidemia, Hypertension & Diabetes mellitus

Conclusions

Previous studies have shown a clear link between testosterone deficiency and ischemic heart disease. In this study, we have found that testosterone deficiency increases the risk for recurrent hospitalization for acute coronary syndrome in people who have been diagnosed with ischemic heart disease. Furthermore, testosterone deficiency may have a negative impact on the risk factors for coronary artery disease like hypertension, diabetes mellitus and hyperlipidemia. This may open the door for future research to highlight the efficacy of testosterone replacement therapy as a secondary prevention for ischemic heart disease.

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