

Serum testosterone levels and Colonic Diverticula

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Received - 4 January 2019

Initial Review – 10 January 2019

Accepted– 2 February 2019

ABSTRACT

Background: Elderly men have a high risk of metabolic syndrome, including an increased risk of obesity. Whether low testosterone is associated with diverticular disease of the colon (DDC) risk independent of metabolic co-factors is not clear. **Aim:** This study was conducted this study to reveal the possible link between serum testosterone levels and colonic diverticula. **Methods:** This study was conducted between May 2018 and December 2018, total 208 subjects were enrolled for the study at a university hospital, Turkey. At total, 85 men with DDC were enrolled for the study. DDC was defined by non-contrast CT scan with colonoscopic examination. Control group (123 subjects without DDC; the mean age was 54.5 ± 14.5) were selected from otherwise healthy men. **Results:** Of the 85 men with DDC, the mean age was 60.8 ± 13.5 years. Lower levels of total testosterone were associated with a 25% increased odds of prevalent DDC on adjusted analyses. Importantly, lower levels of total testosterone remained strongly associated with prevalent DDC, even in men with normal glucose levels ($p=0.01$). **Conclusion:** Decreasing levels of total testosterone, even within normal range, are independently associated with DDC in elderly age. Androgen deficiency may have an important role in the development of DDC in men and provide a potential novel target for DDC prevention.

Key words: Testosterone, colon diverticula, androgen deficiency, obesity.

Diverticular disease of the colon (DDC) is caused by herniation of colonic mucosa and submucosa through the muscularis propria, particularly in weakest areas of the large bowel. Most DDC are uncomplicated but they could cause free perforation and peritonitis which causes higher morbidity and health burden [1]. The prevalence of diverticulosis was 33% in subjects between 50 and 59 years old and 71% in those older than 80 years in the USA [2]. Diverticular bleeding or acute diverticulitis were not associated with well-known risk factors including age, gender, obesity, exercise, fiber intake, alcohol use, constipation, or use of NSAIDs [3].

On the other hand, testosterone deficiency is a common disorder in the elderly male population, with an extremely

high prevalence observed in those with coronary artery disease (CAD), obesity, metabolic syndrome, and type 2 diabetes [4]. Testosterone generally also has a key role involving immunosuppressive and anti-inflammatory events [5]. Furthermore, it has been shown that administration of testosterone following urogenital procedures improves the histologic composition of the urothelium and leads to an increased inflammatory response in the supportive urethral stroma [6]. There is robust evidence that DDC affects at least a quarter of all men with elderly population. DDC also represents an increasing pathology and healthcare burden worldwide and its rates increases annually and with age [7]. Evidence suggests that a deterioration of the host immune response is

associated with both diverticulosis and diverticulitis. This phenomenon may relate to the high prevalence of insulin resistance (IR) and obesity [8].

There is still no data in the literature about the connection between serum testosterone levels and colonic diverticula. Thus, we conducted a retrospective analysis for investigating the association between total testosterone levels and DDC.

METHODS

A small comprehensive retrospective search of the hospital databases was performed from May 2018 to December 2018 in a Turkish tertiary hospital near the coastal region of Blacksea. Total 208 subjects were enrolled in the study after getting ethical clearance from the institute and informed consent from the patients. Among 85 men (the mean age was 54.5 ± 14.5 years; 50% were inpatient) who underwent colonoscopy with at least one total testosterone measurements in the two-year prelude period, we examined the association of total testosterone levels and CD. Baseline laboratory screening and sociodemographic features of the study subjects were also documented.. Control group (123 subjects without DDC) were selected from otherwise healthy men.

The inclusion criterion was the eligibility test results for the serum total testosterone (TT) in subjects with DDC in which detected by colonoscopy and CT of the abdomen. Subjects who were taking testosterone treatment or had prior testicular surgery, urinary system cancer and liver cirrhosis were excluded from the study. We calculated pooled mean difference (MD) and odds ratio (OR) of TT with 95% confidence intervals (CI) comparing between subjects with and without DDC.

RESULTS

Among the total 208 patients, the mean age of study group was 60.8 ± 13.5 and the mean age of control group was the 55 ± 14 years. There were no statistically significant difference between groups in terms of age, laboratory parameters and HbA 1 c levels (all $P > 0.005$). In DDC group; the median total testosterone level was 11.8 nmol/L (normal 10-27.6nmol/L) and 28.1% of men had low total testosterone. While in controls, the median total testosterone level was 21.6 nmol/L (normal 10-27.6nmol/L) and 11.2% of men had low total testosterone. TT levels dominated in the non DDC group in comparison to those having DDC. ($P=0.032$).

Moreover, our study demonstrated significant associations between serum TT with AST and cholesterol levels ($p = 0.014$ and $p = 0.12$, respectively). We also found

that lower TT level was also associated with DDC, independent of haemoglobin A1C levels.

DISCUSSION

Our study supports the importance of serum testosterone levels in assessing DDC. These data may suggest alternate mechanistic pathways and preventive targets in DDC. Our findings were also in line with other studies involving mucosal and wound healing effects of testosterone [3,6]. While DDC is also associated with obesity, it is unclear whether this association is linked to hormonal changes in testosterone levels [9]. In this small study, we revealed a robust association between lower total testosterone levels and DDC.

Some of the previous studies revealed that introducing 5α -DTH was associated with better healing pattern for complete wound closure, and a positive impact on the scar tissue as well as skin wounds repair. This study also suggests that human mucosal healing rates are positively modulated by testosterone level which is similar to previous studies [9-11]. Some researchers also shed light on the fact that testosterone may promote the development of colon cancer via a number of pathways, which may place males at greater risk. Very recently, the measurement of serum free testosterone has been suggested as a novel biomarker in connection with carcinoembryonic antigen in colorectal cancer [12]. Importantly, sex steroids have a modulatory role on the feedback control of gastric motility induced by noxious colonic distension [13,14].

On the metabolic aspect; asymptomatic diverticular disease was associated with age and cardio metabolic risk factors. Subjects with advanced diverticular disease were older and had a higher body mass index (BMI), LDL cholesterol levels and systolic blood pressure [15]. On the other hand, a recent study showed that the BMI greater than 25 kg/m² were associated with an increased incidence and severity of complicated diverticular disease [16]. A recent study conducted among 125 men showed that TT levels were independently predicted by age, insulin, red blood cell aggregation, and transferrin saturation. Those authors also showed that a high consumption of bread and pastries, dairy products, and desserts, eating out, and a low intake of homemade foods, noodles, and dark green vegetables independently predicted hypogonadism [17]. In addition, a causal relationship has also been presented between smoking, obesity, alcohol consumption, low fiber consumption, high meat intake and DDC [18]. We concluded that elderly hypoandrogenic men have a high risk of metabolic syndrome related increased risk of DDC.

There were several limitations of the study. First, results of the study may not be generalized entirely the subjects with DDC due to small sample size. Second, we

did not obtain the BMIs of the study subjects from the data base search due to retrospective nature of the study. This study brags to be the first of its kind in the English literature to show a robust and inverse association between androgens and DD. So, our findings may provide a potential novel target for preventing DDC.

Table 1: Group statistics of patients with and without diverticular disease of the colon

Parameters	DDC Present (n=85)			DDC Absent (n=123)			P value
	Mean	Standart deviation	Standart mean error	Mean	Standart deviation	Standart mean error	
WBC (mm ³)	7.46	3.10	0.33	7.24	7.24	0.22	0.005
Neutrophil (mm ³)	44.73	25.78	2.79	12.19	19.10	1.72	0.005
Hemoglobin(g/dl)	12.95	2.04	0.22	13.21	1.90	0.17	0.005
Hematocrit (%)	40.00	5.87	0.636	40.44	5.05	0.45	0.005
MCV (fL)	86.94	6.83	0.74	86.61	5.98	0.53	0.005
Platelet (10 ⁹ /L)	244.24	75.75	8.21	252.08	75.51	6.80	0.005
Glucose (mg/dL)	126.57	58.50	6.46	108.00	27.74	2.53	0.005
Urea (mg/dl)	36.19	23.80	2.59	33.18	21.28	1.95	0.005
Creatinine (mg/dl)	1.82	8.38	0.90	0.93	0.80	0.072	0.005
AST (U/L)	24.23	32.24	3.56	21.85	9.091	0.83	0.005
ALT (U/L)	22.63	27.76	3.02	20.17	13.41	1.21	0.005
Albumin(g/dl)	4.52	0.41	0.05	4.45	0.57	0.06	0.005
ALP (U/L)	83.77	31.02	4.10	83.21	37.35	3.95	0.005
GGT (U/L)	33.03	41.04	5.48	26.03	22.78	2.41	0.005
Triglycerides(mg/dl)	153.90	137.24	16.28	153.16	85.38	8.41	0.005
HDL-cholesterol (mg/dL)	47.78	14.12	1.69	54.92	58.05	5.80	0.005
LDL-cholesterol (mg/dL)	120.68	39.77	4.78	117.36	37.68	3.80	0.005
Total cholesterol (mg/dl)	197.48	51.98	6.12	185.51	46.30	4.58	0.005
Ferritin (µg/dL)	98.18	45.02	6.78	112.23	245.82	29.59	0.005
TSH (µIU/L)	4.38	20.87	2.41	3.07	2.43	0.23	0.005
HbA1c (%)	6.03	1.53	0.22	5.81	0.96	0.12	0.005

CONCLUSION

Our findings support a key role of androgens as a potential mediator of risk for DDC in men, which may offer potential targets for DDC prevention in elderly population. On the other hand, whether testosterone therapy is associated with NAFLD risk independent of metabolic co-factors is still not clear. It is also unknown whether normal range testosterone levels in men pose an increased risk of DDC. Further studies are needed to determine the specific underlying pathways between testosterone deficiency and DDC in men, and whether administration of testosterone replacement therapy can reduce the prevalence of DDC.

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Funding: None; Conflict of Interest: None Stated.

How to cite this article: Turan R, Yilmaz TE, Goktas TA, Dulger CA, Poyraz B, Yakarısık M. Serum testosterone levels and Colonic Diverticula. *Eastern J of Medical Sciences.* 2019;4(1):29-32.

DOI: 10.32677/EJMS.2019.v04.i01.006