

# Pistachio Diet Improves Erectile Function Parameters and Serum Lipid Profiles in Patients with Erectile Dysfunction

M Aldemir; E Okulu; S Neşelioğlu; O Erel; Ö Kayıgil

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## Abstract and Introduction

### Abstract

We investigated the effects of Antep pistachio on International Index of Erectile Function (IIEF) scores, penile color Doppler ultrasound (PCDU) parameters and serum lipid levels in patients with ED. A total of 17 married male patients with ED for at least 12 months were included in this prospective study. Patients were put on a 100 g pistachio nuts diet for 3 weeks. IIEF and PCDU were evaluated before and after the pistachio diet. In addition, plasma total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglyceride were measured before and after dietary modifications from all subjects. Mean IIEF-15 score was  $36 \pm 7.5$  before the diet and  $54.2 \pm 4.9$  after the diet ( $P=0.001$ ). Similarly, an increase in all five domains of IIEF was observed after the diet ( $P<0.05$ ). Mean peak systolic velocity values before and after the pistachio diet were  $35.5 \pm 15.2$  and  $43.3 \pm 12.4$   $\text{cm s}^{-1}$ , respectively ( $P=0.018$ ). After the pistachio diet, TC and LDL levels decreased significantly, whereas HDL level increased ( $P=0.008$ ,  $0.007$  and  $0.001$ , respectively). We demonstrated that a pistachio diet improved IIEF scores and PCDU parameters without any associated side effects in patients with ED. Furthermore, the lipid parameters showed statistically significant improvements after this diet.

### Introduction

Penile erection is a hemodynamic process involving increased arterial inflow and restricted venous outflow, coordinated with corpus cavernosum and penile arterial smooth muscle relaxation. Any problem in this mechanism results in ED, and its etiology is generally multifactorial.<sup>[1]</sup> Diabetes, hypertension, high serum cholesterol level, peripheral vascular disease and cardiac problems are significantly found together with ED.<sup>[2]</sup> However, vascular reasons predominate in the etiology of ED and it frequently appears along with atherosclerosis.<sup>[2]</sup> It is known that atherosclerotic lesions prevent blood flow into cavernosal tissues resulting in ED.<sup>[3]</sup>

Pistachio (*Pistacia vera* L.), a member of the Anacardiaceae family, is a native of the arid zones of Central and West Asia and distributed throughout the Mediterranean basin. In Turkey, the pistachio is grown mainly in the city of Gaziantep.<sup>[4]</sup> Pistachio nuts are rich sources of plant proteins, dietary fibers and especially antioxidant substances (for example, antioxidant vitamins), besides being high in unsaturated fatty acids and low in saturated fatty acids (Table 1), which may also have cardioprotective effects.<sup>[5,6]</sup> Endothelial dysfunction, characterized by impaired nitric oxide bioavailability, precedes the development of atherosclerotic lesions and has been suggested as an important link between ED and cardiovascular disease.<sup>[7,8]</sup>

**Table 1. Fatty acids, antioxidant vitamins, minerals and some bioactive substances in pistachio nuts per 100 g (dried)<sup>a</sup>**

	Pistachio nuts
SFA (g)	5.44
PUFA (g)	7.31
MUFA (g)	32.6
Vitamin C (mg)	7.19

Vitamin A (IU)	233
Tocopherol- $\alpha$ (mg)	2.30
Tocopherol- $\gamma$ (mg)	22.60
Tocopherol- $\delta$ (mg)	0.80
Phytosterol (mg)	108
Fiber (g)	10.79
Selenium ( $\mu\text{g}$ )	9.39
Arginine (mg)	2.17

Abbreviations: MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

<sup>a</sup><http://nutrition.about.com/library>.

Epidemiological studies have demonstrated an association between nut consumption and coronary heart disease.<sup>[9]</sup> Compared with people who ate nuts less than one time per week, those who ate them 1–4 times per week had a 25% reduced risk of dying from coronary heart disease; people who ate nuts at least 5 times per week showed a 50% reduction in risk.<sup>[10]</sup> The American Heart Association recommends up to 20% of calories from monounsaturated fat and substituting unsaturated fat from vegetables and nuts.<sup>[11]</sup>

Although various studies exist regarding the positive effects of pistachio nuts on serum lipid profiles, to the best of knowledge, its effect on ED has not been investigated yet. In our study, we investigated the effects of pistachio nuts on International Index of Erectile Function (IIEF) scores, penile color Doppler ultrasound (PCDU) and serum lipid levels in patients with ED.

## Materials and Methods

### Design and Patients

A total of 17 married male patients (mean age  $47.9 \pm 6.2$ , range 38–59 years) with ED for at least 12 months were included in the study. All patients were evaluated using medical history and sexual history with IIEF, physical examination and routine blood analysis. IIEF-5 and IIEF-15 questionnaires were applied to all patients.<sup>[12,13]</sup> All five domains (erectile function, orgasmic function, sexual desire, sexual intercourse satisfaction and overall satisfaction) of IIEF were recorded. ED domain score was calculated by the IIEF short form (IIEF-5). Subjects were accepted as having ED if the ED domain score was  $<21$ . Serum fasting blood glucose, total testosterone levels and lipid profiles were measured in the routine blood analysis for the diagnosis of ED. Lipid profiles of the patients included in our study are presented in Table 2.

**Table 2. Summary of patient serum lipid profiles**

	N (%)
TC $<200 \text{ mg dl}^{-1}$	11 (64.7)
TC between 200 and $240 \text{ mg dl}^{-1}$	2 (11.8)
TC $>240 \text{ mg dl}^{-1}$	4 (23.5)
TG $<200 \text{ mg dl}^{-1}$	13 (76.5)
TG $>200 \text{ mg dl}^{-1}$	4 (23.5)

LDL <135 mg dl <sup>-1</sup>	15 (88)
LDL >135 mg dl <sup>-1</sup>	2 (11.8)
HDL <35 mg dl <sup>-1</sup>	3 (17.6)
HDL >35 mg dl <sup>-1</sup>	14 (82.4)

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

The study did not include those patients who had a systemic disease such as malignancy, hepatic or renal failure, coronary artery disease, active infection; those who underwent any operation or cardiovascular intervention within the previous 3 months; and those who underwent any medical treatment such as intake of phosphodiesterase type 5 inhibitors, multivitamin drugs,  $\beta$ -blockers, thiazide diuretics and lipid-lowering drugs in the last 3 months. Patients with secondary hyperlipidemia, hypothyroidism, nephrotic syndrome, dysglobulinemias, Cushing's syndrome, vascular impairments, hypertension and angina were excluded.

After the approval of the local ethic committee, patients were informed about the study and gave signed consent.

Previous studies have used 60–100 g of pistachios per day for a period of 3 to 4 weeks.<sup>[6,14,15]</sup> Therefore, in this study, our patients received 100 g of pistachio nuts per day for a period of 3 weeks. Patients consumed 100 g of pistachio nuts at lunch every day for a period of 3 weeks. This corresponds to 20% (570 kcal) of the daily calorie intake. The subjects were informed to maintain similar daily dietary intake, similar physical activity and other lifestyle habits. No subjects were reported to have side effects during the pistachio-diet period and no patient dropped out during the study.

Before the pistachio diet, body mass index, systemic systolic and diastolic blood pressures, fasting blood glucose level, lipid parameters and blood testosterone levels were measured. Basal serum prolactin levels of our patients were measured in order to detect presence of hyperprolactinemia as a possible etiological factor of ED. IIEF-5 and IIEF-15 scores were determined and PCDU was performed. At the end of 3 weeks, all of these tests were repeated and the results were compared with the results obtained before the diet.

### PCDU Measurements

PCDU was performed using a linear probe (B-K Medical, Herlev, Denmark) with 8 MHz frequency to diagnose the arterial or veno-occlusive pathology. PCDU measurements were performed by the same radiologist. Before the test, papaverine HCl (60 mg) was injected into one of the cavernosal bodies. Thereafter, peak systolic velocity (PSV) and end diastolic velocity (EDV) were taken separately from right and left cavernosal arteries. Measurement of PSV at 20 min of intracavernosal injection was reported to be sufficient.<sup>[16]</sup> Therefore, we measured PSV following 20 min of intracavernosal injection. The resistive index (RI) of each cavernosal artery was calculated individually using the formula:  $RI = \frac{PSV - EDV}{PSV}$ .

### Serum Lipid Profile Measurements

Heparinized blood samples were obtained from all subjects after an overnight fast before and after the pistachio diet. The levels of triglyceride (TG), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and fasting glucose were determined using a colorimetric method (Advia; Siemens, Erlangen, Germany) with an automatic analyzer (Siemens, Germany).

### Statistical Analysis

SPSS version 11.5 software (Chicago, IL, USA) was used for data analysis. Continuous variables were expressed as mean  $\pm$  s.d. Kolmogorov–Smirnov test was used for a normal distribution before analysis. Two-tailed *t*-test for paired

samples was used to compare changes in outcome variables in response to pistachio diet. Because similar parameters of the same patients were measured in different time intervals (that is, before and after the pistachio diet), paired-samples *t*-test was used in our study. The *P*-values <0.05 were considered significant.

## Results

All 17 patients completed the study and none of them experienced side effects during the study. The mean age was 47.9±6.2 (range 38–59) years. Mean body mass index was 27.33±2.88 and did not change after the pistachio diet (*P*<0.05). Systemic systolic and diastolic blood pressure values were similar before and after the diet (*P*<0.05).

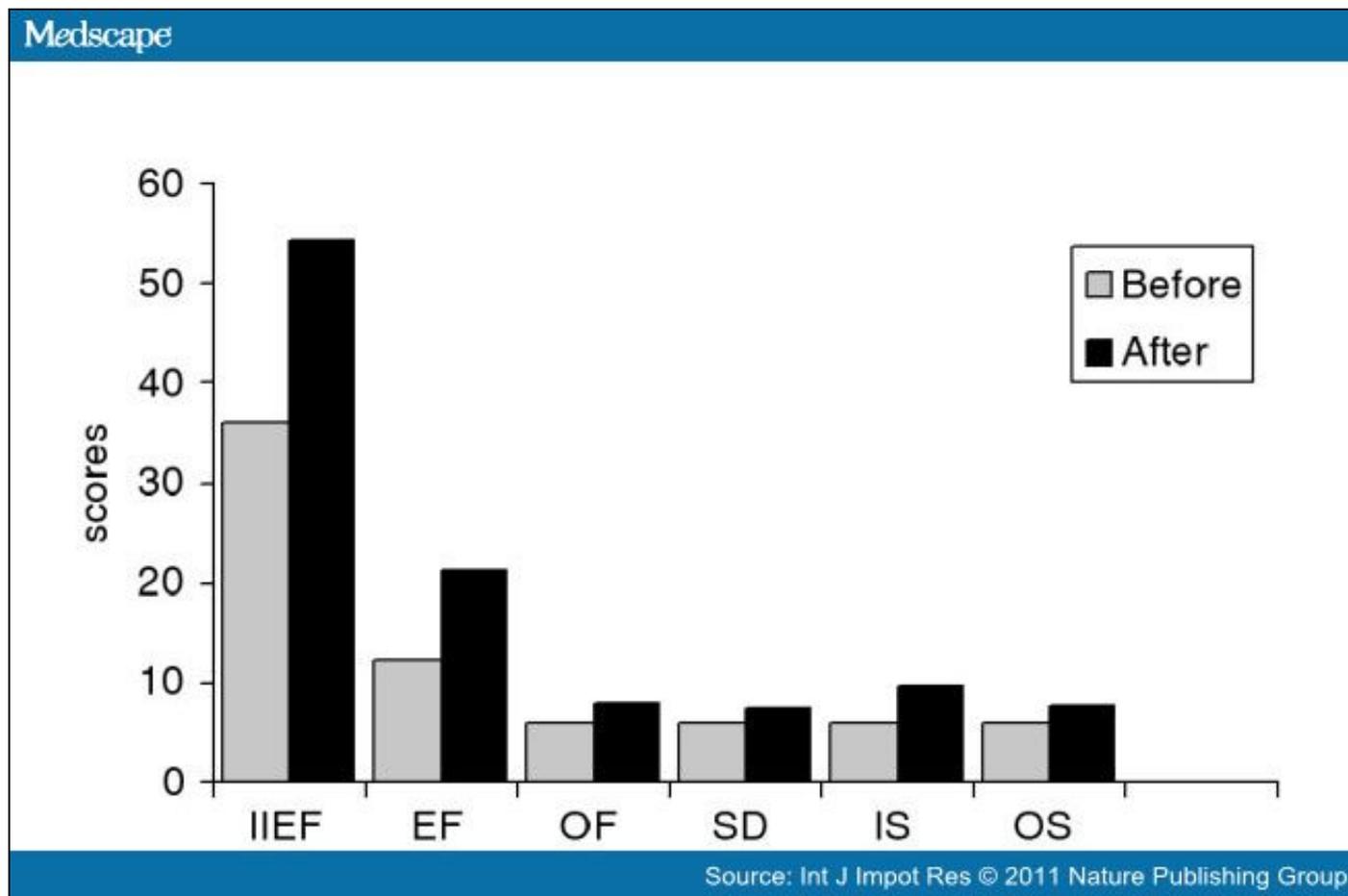
Before the diet, mean IIEF-5 score of the patients was 10.5±3.1. Total IIEF-15 score was 36±7.5 before the diet and 54.2±4.9 after the diet (*P*=0.001). Similarly, all of the five domains of IIEF-15 showed a statistically significant increase (*P*<0.05; Table 3 and Figure 1).

**Table 3. The results of total IIEF-15 and five domain scores before and after the pistachio diet**

Parameters	Before the pistachio diet, mean±s.d. (n=17)	After the pistachio diet, mean±s.d. (n=17)	P-value <sup>a</sup>
Total IIEF-15	36±7.5	54.2±4.9	0.001
EF	12.1±3	21.4±2.3	0.001
OF	5.9±1.4	8.1±0.8	0.001
SD	5.9±2.1	7.4±1.9	0.008
IS	6.1±1.4	9.8±1.3	0.001
OS	6±1.7	7.6±1.4	0.001

Abbreviations: EF, erectile function; IIEF, International Index of Erectile Function; IS, sexual intercourse satisfaction; OF, orgasmic function; OS, overall satisfaction; SD, sexual desire.

<sup>a</sup>Paired-samples *t*-test was used.



**Figure 1.** Total IIEF and the five domain score findings before and after the pistachio diet. EF, erectile function; IIEF, International Index of Erectile Function; IS, sexual intercourse satisfaction; OF, orgasmic function; OS, overall satisfaction; SD, sexual desire.

Based on the results obtained from the PCDU, mean PSV of the patients was  $35.5 \pm 15.2 \text{ cm s}^{-1}$  before the diet and  $43.3 \pm 12.4 \text{ cm s}^{-1}$  after the diet ( $P=0.018$ ). Although not statistically significant, the values of EDV showed an improvement after the pistachio diet ( $P=0.401$ ). Other results obtained from PCDU are shown in Table 4.

**Table 4. Results of PCDU of the patients before and after the pistachio diet**

Parameters	Before the pistachio diet, mean $\pm$ s.d. (n=17)	After the pistachio diet, mean $\pm$ s.d. (n=17)	P-value <sup>a</sup>
Tumescence (grade)	1.9 $\pm$ 0.9	3.4 $\pm$ 0.6	0.001
Right PSV (cm s <sup>-1</sup> )	34.9 $\pm$ 14.4	41.1 $\pm$ 14.4	0.079
Left PSV (cm s <sup>-1</sup> )	36 $\pm$ 16.3	45.4 $\pm$ 12.7	0.011
Mean PSV (cm s <sup>-1</sup> )	35.5 $\pm$ 15.2	43.3 $\pm$ 12.4	0.018
Right EDV (cm s <sup>-1</sup> )	4.8 $\pm$ 7.6	3 $\pm$ 1.6	0.309
Left EDV (cm s <sup>-1</sup> )	3.9 $\pm$ 7.4	2.8 $\pm$ 1.6	0.540

Mean EDV (cm s <sup>-1</sup> )	4.3±7.3	2.9±1.5	0.401
Right RI	0.8±0.1	0.9±0.1	0.005
Left RI	0.8±0.2	0.9±0.1	0.003
Mean RI	1±0.1	0.9±0.1	0.134

Abbreviations: EDV, end-diastolic velocity; PCDU, penile color Doppler ultrasound; PSV, peak systolic velocity; RI, resistive index.

<sup>a</sup> Paired-samples *t*-test was used.

After the pistachio diet, TC and LDL levels showed a significant decrease ( $P=0.008$  and  $P=0.007$ ). TC/HDL and LDL/HDL rates showed a significant decrease after the pistachio diet ( $P=0.001$ ), whereas HDL level showed a significant increase after the pistachio diet ( $P=0.001$ ). TG/HDL ratio showed a significant decrease after the pistachio diet ( $P=0.013$ ; Table 5 and Figure 2).

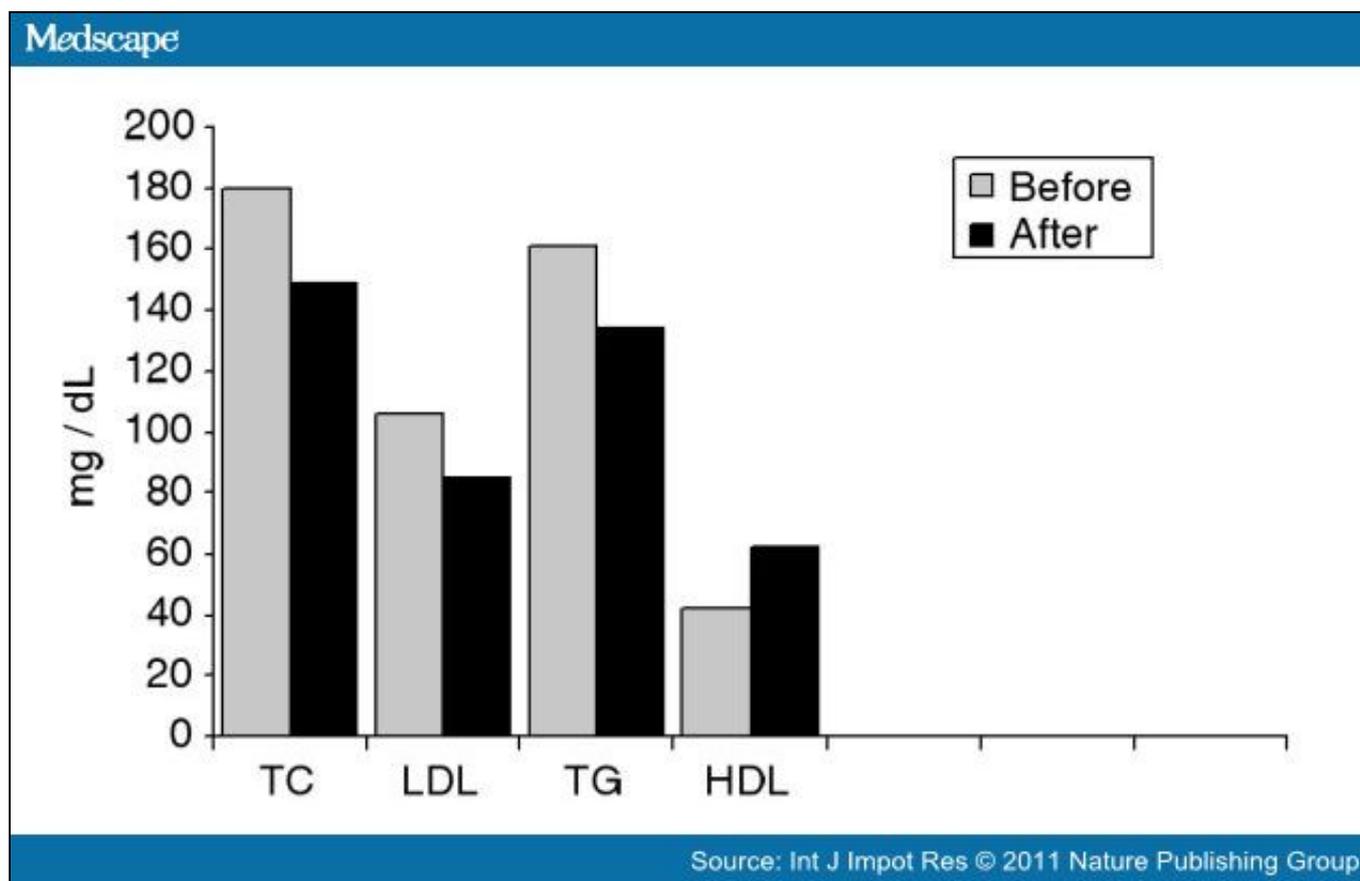
**Table 5. Summary of serum lipid levels and other biochemical parameters before and after the pistachio diet**

	Before the pistachio diet, mean±s.d. (n=17)	After the pistachio diet, mean±s.d. (n=17)	P-value <sup>a</sup>
TC (mg dl <sup>-1</sup> )	179.5±53.2	148.3±38.9	0.008
TG (mg dl <sup>-1</sup> )	160.8±99	133.9±71.1	0.288
HDL (mg dl <sup>-1</sup> )	42±6.4	62.1±7.9	0.001
LDL (mg dl <sup>-1</sup> )	106.1±30	84.8±10.1	0.007
TC/HDL	4.3±1.4	2.4±0.6	0.001
LDL/HDL	2.6±0.8	1.4±0.2	0.001
TG/HDL	4±2.9	2.1±0.9	0.013
PSA (ng ml <sup>-1</sup> )	0.9±0.5	1±0.7	0.669
Prolactin (ng ml <sup>-1</sup> )	8.8±5	9.2±3.8	0.817
Total testosterone (ng dl <sup>-1</sup> )	452.1±163.4	379.1±95	0.030
Glucose (mg dl <sup>-1</sup> )	102.4±18.3	104.7±19.1	0.487
Urea (mg dl <sup>-1</sup> )	27.1±7.3	27.9±4.8	0.651
Creatinine (mg dl <sup>-1</sup> )	1±0.1	1±0.1	0.579
Leukocyte (K μl <sup>-1</sup> ) ( × 10 <sup>3</sup> )	7±1.8	6.5±1.7	0.144
Hemoglobin (g dl <sup>-1</sup> )	14.7±0.8	14.9±1	0.276
Platelet (K μl <sup>-1</sup> ) ( × 10 <sup>3</sup> )	305.6±85.1	242.4±58.9	0.028

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; PSA, prostate-specific

antigen; TC, total cholesterol; TG, triglyceride.

<sup>a</sup>Paired-samples *t*-test was used.



**Figure 2.** The improvements in lipid levels observed after the pistachio diet. HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

Mean basal total testosterone levels were  $452.1 \pm 163.4$  and  $379.1 \pm 95$  ng  $\text{dl}^{-1}$  before and after the diet, respectively ( $P=0.030$ ). In addition, blood platelet counts showed a significant decrease after the diet ( $P=0.028$ ). Pistachio diet was not found to affect serum prolactin levels. Other biochemical variables obtained before and after the pistachio diet are shown in Table 5.

**Table 5. Summary of serum lipid levels and other biochemical parameters before and after the pistachio diet**

	Before the pistachio diet, mean $\pm$ s.d. (n=17)	After the pistachio diet, mean $\pm$ s.d. (n=17)	P-value <sup>a</sup>
TC (mg $\text{dl}^{-1}$ )	179.5 $\pm$ 53.2	148.3 $\pm$ 38.9	0.008
TG (mg $\text{dl}^{-1}$ )	160.8 $\pm$ 99	133.9 $\pm$ 71.1	0.288
HDL (mg $\text{dl}^{-1}$ )	42 $\pm$ 6.4	62.1 $\pm$ 7.9	0.001
LDL (mg $\text{dl}^{-1}$ )	106.1 $\pm$ 30	84.8 $\pm$ 10.1	0.007
TC/HDL	4.3 $\pm$ 1.4	2.4 $\pm$ 0.6	0.001
LDL/HDL	2.6 $\pm$ 0.8	1.4 $\pm$ 0.2	0.001

TG/HDL	4±2.9	2.1±0.9	0.013
PSA (ng ml <sup>-1</sup> )	0.9±0.5	1±0.7	0.669
Prolactin (ng ml <sup>-1</sup> )	8.8±5	9.2±3.8	0.817
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Urea (mg dl <sup>-1</sup> )	27.1±7.3	27.9±4.8	0.651
Creatinine (mg dl <sup>-1</sup> )	1±0.1	1±0.1	0.579
Leukocyte (K μl <sup>-1</sup> ) ( × 10 <sup>3</sup> )	7±1.8	6.5±1.7	0.144
Hemoglobin (g dl <sup>-1</sup> )	14.7±0.8	14.9±1	0.276
Platelet (K μl <sup>-1</sup> ) ( × 10 <sup>3</sup> )	305.6±85.1	242.4±58.9	0.028

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; PSA, prostate-specific antigen; TC, total cholesterol; TG, triglyceride.

<sup>a</sup>Paired-samples *t*-test was used.

## Discussion

After a pistachio diet of 3 weeks, total IIEF scores and five domains showed a statistically significant increase (Table 3). PCDU of patients showed a statistically significant increase in the value of PSV. EDV showed an improvement but it was not statistically significant (Table 4), which may be attributed to the small number of cases.

**Table 3. The results of total IIEF-15 and five domain scores before and after the pistachio diet**

Parameters	Before the pistachio diet, mean±s.d. (n=17)	After the pistachio diet, mean±s.d. (n=17)	P-value <sup>a</sup>
Total IIEF-15	36±7.5	54.2±4.9	0.001
EF	12.1±3	21.4±2.3	0.001
OF	5.9±1.4	8.1±0.8	0.001
SD	5.9±2.1	7.4±1.9	0.008
IS	6.1±1.4	9.8±1.3	0.001
OS	6±1.7	7.6±1.4	0.001

Abbreviations: EF, erectile function; IIEF, International Index of Erectile Function; IS, sexual intercourse satisfaction; OF, orgasmic function; OS, overall satisfaction; SD, sexual desire.

<sup>a</sup>Paired-samples *t*-test was used.

**Table 4. Results of PCDU of the patients before and after the pistachio diet**

Parameters	Before the pistachio diet, mean±s.d.	After the pistachio diet, mean±s.d.	P-
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Parameters	(n=17)	(n=17)	value <sup>a</sup>
Tumescence (grade)	1.9±0.9	3.4±0.6	0.001
Right PSV (cm s <sup>-1</sup> )	34.9±14.4	41.1±14.4	0.079
Left PSV (cm s <sup>-1</sup> )	36±16.3	45.4±12.7	0.011
Mean PSV (cm s <sup>-1</sup> )	35.5±15.2	43.3±12.4	0.018
Right EDV (cm s <sup>-1</sup> )	4.8±7.6	3±1.6	0.309
Left EDV (cm s <sup>-1</sup> )	3.9±7.4	2.8±1.6	0.540
Mean EDV (cm s <sup>-1</sup> )	4.3±7.3	2.9±1.5	0.401
Right RI	0.8±0.1	0.9±0.1	0.005
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Mean RI	1±0.1	0.9±0.1	0.134

Abbreviations: EDV, end-diastolic velocity; PCDU, penile color Doppler ultrasound; PSV, peak systolic velocity; RI, resistive index.

<sup>a</sup> Paired-samples *t*-test was used.

Pistachio nuts are rich sources of some plant proteins, dietary fibers and especially antioxidant substances, besides being high in unsaturated fatty acids and saturated fatty acids (Table 1). In addition, pistachio nuts are relatively high in the nonessential amino acid arginine, which appears to maintain flexible arteries and to enhance blood flow by boosting nitric oxide, a compound that relaxes blood vessels.<sup>[17]</sup> Sari *et al.* <sup>[6]</sup> demonstrated that a pistachio diet resulted in an improvement in endothelium-dependent vasodilation in normolipidemic healthy young men. Improvement of blood vessel relaxation and endothelium-dependent vasodilatation might be related with significantly increased PSV values in PCDU in our study.

**Table 1. Fatty acids, antioxidant vitamins, minerals and some bioactive substances in pistachio nuts per 100 g (dried)<sup>a</sup>**

	Pistachio nuts
SFA (g)	5.44
PUFA (g)	7.31
MUFA (g)	32.6
Vitamin C (mg)	7.19
Vitamin A (IU)	233
Tocopherol- $\alpha$ (mg)	2.30
Tocopherol- $\gamma$ (mg)	22.60
Tocopherol- $\delta$ (mg)	0.80

Phytosterol (mg)	108
Fiber (g)	10.79
Selenium (µg)	9.39
Arginine (mg)	2.17

Abbreviations: MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid.

<sup>a</sup><http://nutrition.about.com/library>.

Oxidative stress decreased synthesis and bioavailability of endothelial and neuronal nitric oxide.<sup>[18]</sup> We know that pistachio nuts are rich sources of antioxidant substances (Table 1). Kocyigit *et al.*<sup>[14]</sup> reported that a 3-week pistachio diet in healthy volunteers had a favorable effect on oxidative stress. They found a decrease in malondialdehyde level and an increase in antioxidant potential. Serum interleukin-6, total oxidant status, lipid hydroperoxide and malondialdehyde levels were detected to be decreased following administration of 60–100 g pistachio diet for 4 weeks in another study.<sup>[6]</sup> The antioxidant effects of pistachio against oxidative damage might originate from phytochemicals in its content as resveratrol and anthocyanins have strong free radical scavenging ability.<sup>[14,19]</sup>

**Table 1. Fatty acids, antioxidant vitamins, minerals and some bioactive substances in pistachio nuts per 100 g (dried)<sup>a</sup>**

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<sup>a</sup><http://nutrition.about.com/library>.

PON1 (paraoxonase 1) and arylesterase, the HDL-bound enzyme system, are well-known antioxidant molecules. This enzyme system protects LDL and HDL from oxidation by hydrolyzing activated phospholipids and lipid peroxide products, and thus prevents atherosclerosis. Additionally, PON1 activity was suggested to modulate endothelial functions.<sup>[20]</sup> Ciftci *et al.*<sup>[21]</sup> reported that the PON1 activity was found significantly lower in patients with ED

compared with the control group.

Aksoy *et al.* [22] used 20 and 40% of daily caloric intake pistachio diet for 10 weeks in an experimental study in rats. Consumption of pistachio as 20% of daily caloric intake resulted in a significant improvement in HDL cholesterol and TC/HDL ratio. Moreover, consumption of pistachio as 20% of daily caloric intake increased PON1 activity by 35% and arylesterase activity by 60%, which inhibits oxidation of LDL cholesterol. They also found out that consumption of pistachio as 20% of daily caloric intake resulted in better outcomes compared with 40% of daily caloric intake.

The association between hyperlipidemia and ED is originally attributed to atherosclerosis in the hypogastric-cavernosal arterial bed, with a subsequent insufficiency in penile arterial inflow.[23] Impairment of endothelium-dependent relaxation in numerous vascular beds in men with hypercholesterolemia has been firmly established.[24–26] These impairments have also been shown to be reversible, using lipid-lowering therapies.[27] Another study related to this subject showed that the association between hyperlipidemia and ED is attributed to the impairment of endothelium-dependent relaxation in smooth muscle cells of corpus cavernosum by hypercholesterolemia.[28] Wei *et al.* [29] demonstrated that a high level of TC and a low level of HDL are important risk factors for ED. In this study, every mmol l<sup>-1</sup> increase in TC was associated with a 1.32-fold increase in the risk of ED. Men with TC >240 mg dl<sup>-1</sup> had 1.83 times the risk than did men with <180 mg dl<sup>-1</sup>. [29] Pinnock *et al.* [30] showed that high cholesterol level was an independent predictor of impotence. Manning *et al.* [31] found a correlation between high LDL and organic ED (68.6 vs 32.4% in the psychogenic impotence group), and a clear positive correlation between high LDL and cavernous insufficiency was determined. Nikoobakht *et al.* [32] demonstrated that there was a significant correlation between total cholesterol and LDL with ED. According to this study, every mg dl<sup>-1</sup> increase in plasma cholesterol and LDL levels decreased IIEF-5 scores by 0.036 and 0.035, respectively. Improvement of serum lipid profiles might be related with increase in IIEF scores in our study.

Another study showed HDL and TC/HDL ratio as significant predictors of ED.[33] It was also stated that decreased serum lipid levels might have contributed to penile tumescence.[33] All these studies suggest a relationship between serum lipid profiles and ED. Improvement in serum lipid profiles seems to also improve erectile functions.

Previous studies about the effect of pistachio on lipid parameters have shown favorable effects.[11,14,15] Sheridan *et al.* [11] reported that 4 weeks of pistachio diet as 15% of daily caloric intake caused significant decreases in TC/HDL ratio (from 4.7 to 4.4) and LDL/HDL ratio (from 3.1 to 2.8) along with a significant increase in HDL (from 55 to 57 mg dl<sup>-1</sup>) in subjects with moderate hypercholesterolemia. Kocyigit *et al.* [14] reported that 3 weeks of pistachio diet as 20% of daily caloric intake caused significant decreases in TC levels (from 4.08±0.69 to 3.61±0.60 mmol l<sup>-1</sup>) and TC/HDL (from 3.98±1.41 to 3.17±1.04) and LDL/HDL (from 1.82±0.51 to 1.58±0.47) ratios, and a significant increase in HDL (from 1.01±0.28 to 1.28±0.27 mmol l<sup>-1</sup>) in normolipidemic healthy volunteers. TG and LDL levels were found to be unchanged.[14] Edwards *et al.* [15] demonstrated that 3 weeks of pistachio diet as 20% of daily caloric intake caused significant decreases in TC (from 243 to 239 mg dl<sup>-1</sup>), TC/HDL ratio (from 4.8 to 4.5) and LDL/HDL ratio (from 3.2 to 3.1), and a significant increase in HDL (from 50 to 56 mg dl<sup>-1</sup>) in moderately hypercholesterolemic patients, whereas TG and LDL levels remained unchanged.

In our study, we observed a significant decrease in TC (from 179.5 to 148.3 mg dl<sup>-1</sup>) levels, LDL (from 106.1 to 84.8 mg dl<sup>-1</sup>) and TC/HDL (from 4.3 to 2.4) and LDL/HDL (from 2.6±to 1.4) ratios, and an increase in HDL (from 42 to 62.1 mg dl<sup>-1</sup>) levels among pistachio nuts consumers. Although statistically not significant, a decrease in TG levels was found. In addition, TG/HDL ratio (from 4 to 2.1) was significantly decreased (Table 5). To the best of our knowledge, our study is the first that demonstrated that pistachio nuts decreases serum TG/HDL ratio.

**Table 5. Summary of serum lipid levels and other biochemical parameters before and after the pistachio diet**

	Before the pistachio diet, mean±s.d. (n=17)	After the pistachio diet, mean±s.d. (n=17)	P-value <sup>a</sup>

TC (mg dl <sup>-1</sup> )	179.5±53.2	148.3±38.9	0.008
TG (mg dl <sup>-1</sup> )	160.8±99	133.9±71.1	0.288
HDL (mg dl <sup>-1</sup> )	42±6.4	62.1±7.9	0.001
LDL (mg dl <sup>-1</sup> )	106.1±30	84.8±10.1	0.007
TC/HDL	4.3±1.4	2.4±0.6	0.001
LDL/HDL	2.6±0.8	1.4±0.2	0.001
TG/HDL	4±2.9	2.1±0.9	0.013
PSA (ng ml <sup>-1</sup> )	0.9±0.5	1±0.7	0.669
Prolactin (ng ml <sup>-1</sup> )	8.8±5	9.2±3.8	0.817
Total testosterone (ng dl <sup>-1</sup> )	452.1±163.4	379.1±95	0.030
Glucose (mg dl <sup>-1</sup> )	102.4±18.3	104.7±19.1	0.487
Urea (mg dl <sup>-1</sup> )	27.1±7.3	27.9±4.8	0.651
Creatinine (mg dl <sup>-1</sup> )	1±0.1	1±0.1	0.579
Leukocyte (K μl <sup>-1</sup> ) ( × 10 <sup>3</sup> )	7±1.8	6.5±1.7	0.144
Hemoglobin (g dl <sup>-1</sup> )	14.7±0.8	14.9±1	0.276
Platelet (K μl <sup>-1</sup> ) ( × 10 <sup>3</sup> )	305.6±85.1	242.4±58.9	0.028

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; PSA, prostate-specific antigen; TC, total cholesterol; TG, triglyceride.

<sup>a</sup>Paired-samples *t*-test was used.

Similar to the previous studies, we used pistachio diet for 3-week duration. However, in our study, patients only consumed the pistachio diet during lunch, in order to provide maximum absorption. This was different than the other studies. More than 50% of our patients were normolipidemic and rest of them was hyperlipidemic (Table 2). Following 3-week pistachio diet, improvement in lipid profiles was detected in all patients.

**Table 2. Summary of patient serum lipid profiles**

	<b>N (%)</b>
TC <200 mg dl <sup>-1</sup>	11 (64.7)
TC between 200 and 240 mg dl <sup>-1</sup>	2 (11.8)
TC >240 mg dl <sup>-1</sup>	4 (23.5)
TG <200 mg dl <sup>-1</sup>	13 (76.5)
TG >200 mg dl <sup>-1</sup>	4 (23.5)
LDL <135 mg dl <sup>-1</sup>	15 (88)
LDL >135 mg dl <sup>-1</sup>	2 (11.8)

HDL <35 mg dl <sup>-1</sup>	3 (17.6)
HDL >35 mg dl <sup>-1</sup>	14 (82.4)

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride.

Several hypotheses have been suggested for the serum lipid-lowering effect of pistachio nuts. Pistachio nuts are generally low in saturated fatty acids and high in unsaturated fatty acids. Unsaturated fatty acids (both monounsaturated and polyunsaturated) have been shown to reduce serum TC and LDL. In addition, pistachio nuts contain significant amounts of phytosterols. The major phytosterol component is  $\beta$ -sitosterol, which is one of several plant sterols implicated in cholesterol lowering.<sup>[34]</sup>

Edwards *et al.*<sup>[15]</sup> showed that the decrease in cholesterol could be attributed to the intake of high soluble fiber and phytosterols. Soluble fibers and other plant proteins, such as soy proteins found in pistachio nuts, also increase the level of HDL cholesterol.<sup>[35]</sup> Arginine may account for the hypocholesterolemic effect observed in animal studies.<sup>[36]</sup>

In our study, significant decrease in serum testosterone levels was detected in patients who had pistachio diet (from 452.1 to 379.1 ng dl<sup>-1</sup>). Pistachios are known to have phytosterol. Animal models show that a high intake of phytosterols will reduce serum testosterone levels.<sup>[37]</sup>

Platelets have been suggested to have a role in the pathogenesis of ED. Particularly in vasculogenic ED, platelets were suggested to stick to the cavernosal walls and secrete mediators, leading to an increase in oxidative stress during erection.<sup>[38]</sup> In our study, significant decrease in blood platelet counts were detected following pistachio diet (from 305.6 to 242.4). To the best of our knowledge, this particular effect of pistachio nuts is demonstrated only in our study. Decrease in platelet count might lead to improved blood flow and improvement in PCDU parameters.

As pistachio nuts are fatty food, the consumers may have concerns about gaining weight. However, in our study, we observed that body mass index did not show a change before or after the pistachio diet. Similar to our study, previous studies demonstrated that people who consume up to 20% of the daily calorie intake did not show an increase in body mass index and weight gain.<sup>[6,14]</sup>

## Conclusions

We have shown that 3-week pistachio diet applied to patients with ED resulted in a significant improvement in erectile function parameters (PCDU parameters and IIEF scores) with additional improvement in serum lipid parameters without any side effects. Further studies are needed with increased number of patients and longer follow-up evaluating the relationship between pistachio nuts and ED pathogenesis.

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**Conflict of interest**

The authors declare no conflict of interest.

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