ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

DOI: 10.5336/urology.2021-81576

Evaluation of the Association Between Acute-to-Chronic Glycemic Ratio and Erectile Dysfunction in Diabetic Men: A Retrospective Case-Control Study

Diabetes Mellituslu Erkek Hastalarda Akut-Kronik Glisemik Oran ile Erektil Disfonksiyon Arasındaki İlişkinin Değerlendirilmesi: Retrospektif, Olgu-Kontrol Çalışması

Emre KARABAY[a], Kemal KAYAR[a], Çağatay TOSUN[a]

[a]Department of Urology, University of Health Sciences Haydarpaşa Numune Training and Research Hospital, İstanbul, TÜRKİYE

ABSTRACT Objective: The aim of this study was to investigate the possible association between the acute to chronic (A/C) glycemic ratio and the presence of erectile dysfunction (ED) in diabetic men. **Material and Methods:** A total of 104 diabetic men, 45 of whom had ED while 59 did not, were retrospectively enrolled in this study. Clinical examination and laboratory analyses including A/C glycemic ratio, serum fasting glucose, hemoglobin A1c, lipid profile, and total testosterone were analyzed. **Results:** The total testosterone levels were lower in the diabetic ED patients compared to the non-ED diabetic participants (4.49 ng/dL vs 4.80 ng/dL, respectively). However, the difference was not statistically significant (p=0.093). Mean high-density lipoprotein cholesterol levels were significantly lower in the diabetic ED patients than in the controls (40±9 mg/dL vs 44±10 mg/dL; respectively; p=0.030). Although the median A/C glycemic ratios were higher in the diabetic ED patients (1.28±0.23 vs. 1.18±0.32), no statistical significant differences were noted between the two groups (p=0.054) **Conclusion:** The strong relationship between diabetes mellitus (DM) and ED demands caution since DM is a common disease in the population. We believe that developing biomarkers for the early diagnosis of ED will help provide treatment and improve the life quality of patients. Although we could not find a statistical relationship between the A/C glycemic ratio and ED in our study results, we think that further well-designed prospective studies are needed in this area.

Keywords: Acute to chronic glycemic ratio; diabetes mellitus; erectile dysfunction

ÖZET Amaç: Bu çalışmanın amacı, diyabetik erkeklerde akut-kronik (A/K) glisemik oran ile erektil disfonksiyon (ED) arasındaki muhtemel ilişkiyi araştırmaktır. **Gereç ve Yöntemler:** Kırk beşinde ED olan 59'unda olmayan toplam 104 diyabetik erkek retrospektif olarak çalışmaya dâhil edildi. Klinik muayeneleri ve A/K glisemik oranı, serum açlık glukoz, hemoglobin A1c, lipid profili ve total testosteron düzeyleri dâhil olmak üzere laboratuvar bulguları incelendi. **Bulgular:** Total testosteron düzeyleri diyabetik ED hastalarında ED olmayan diyabetik katılımcılara göre daha düşüktü (4,49 ng/dL vs 4,80 ng/dL, sırasıyla) ancak bu fark istatistiksel olarak anlamlı değildi (p=0,093). Ortalama yüksek-yoğunluklu lipoprotein kolesterol düzeyleri diyabetik ED hastalarında kontrollere göre anlamlı olarak daha düşüktü (40±9 mg/dL vs 44±10 mg/dL; sırasıyla; p=0,030). Ortanca A/K glisemik oranları ED hastalarında daha yüksek olsa da (1,28±0,23 vs. 1,18±0,32), 2 grup arasında istatistiksel anlamlı farklılık izlenmedi (p=0,054). **Sonuç:** Diabetes mellitus (DM) ve ED arasındaki güçlü bir bağ bulunması ve DM'nin toplumda sık bir hastalık olması sebebiyle bu ilişkiye dikkat edilmelidir. ED'nin erken tanısı için biyobelirteçler geliştirmenin tedavide ve hastaların yaşam kalitesini artırmada yardımcı olacağına inanıyoruz. Çalışma sonuçlarımızda, A/K glisemik oranı ve ED arasında istatistiksel anlamlı ilişki bulamasak da bu konuda gelecekte iyi tasarlanmış prospektif çalışmalara ihtiyaç duyulduğu düşüncesindeyiz.

Anahtar Kelimeler: Akut-kronik glisemik oran; diyabetes mellitus; erektil disfonksiyon

Erectile dysfunction (ED) is a common sexual dysfunction of men, in which there is a failure in achieving adequate penile erection for the sexual intercourse.[1,2] Several factors have been shown to be related with the development of ED, such as aging, smoking, diabetes mellitus (DM), cardiovascular disorders (CVD), hypertension (HT), anxiety, and depression, among which DM is considered as a major

Correspondence: Emre KARABAY
Department of Urology, University of Health Sciences Haydarpaşa Numune Training and Research Hospital, İstanbul, TÜRKİYE/TURKEY
E-mail: emrekarabay@gmail.com

Peer review under responsibility of Journal of Reconstructive Urology.

Received: 23 Jan 2021 ***Received in revised form:*** 23 Feb 2021 ***Accepted:*** 25 Feb 2021 ***Available online:*** 03 Mar 2021

determinant.[3-5] The increased risk of ED among diabetic men has been well established. It is thought that 75% of diabetic men will experience ED at some point in their lifetimes, probably at a younger time compared with the non-diabetic population.[6] It was also reported that diabetic men are more likely to have ED compared with non-diabetic males.[7] Various mechanisms contribute to the pathophysiology of ED in DM, such as impaired endothelial function, neuropathy, cummulation of glycation and oxidation products.[8]

ED is an important health issue that causes impairment in the life quality of patients, and it causes an extra burden on the health care systems. Early prediction of ED in diabetic patients may increase the treatment success. Recently, a novel index called the acute-to-chronic (A/C) glycemic ratio has been introduced. The A/C glycemic ratio is calculated by dividing the admission blood glucose (ABG) glycemic value by the chronic [based on glycated hemoglobin (HbA1c)] glycemic value. The A/C ratio is considered a more valuable prognostic marker than diabetes status and acute or chronic glycemic values alone.[9,10]

Thus, the aim of this study was to assess whether there is a relationship the between the A/C glycemic ratio and the presence of ED in men with DM.

MATERIAL AND METHODS

A total of 104 patients were retrospectively enrolled between January 2019 and October 2020 in this study. Forty-five of the subjects were ED patients who were also diagnosed with DM, and 59 age-matched diabetic patients without ED (who were administered to our department for transurethral resection) comprised the control group. All the subjects had type 2 DM. The description of ED was made based on the results of the validated Turkish version of the 15-item International Index of Erectile Function (IIEF-15) survey. Erectile function domain total score <26 defined the parameter for ED.[11] All steps of the study were planned and performed according to the World Medical Association Declaration of Helsinki. All patients signed the informed consent demonstrating the permission of the patients for usage of their clinical data in future clinical studies. Ethical approval was approved by the local ethics comittee of University of Health Sciences, Haydarpaşa Numune Training and Research Hospital (HNEAK-KAEK 2021/KK/34).

A clinical evaluation was performed for all the patients. Demographic features, smoking habits, and the DM and HT status of the patients were recorded. The body mass index (BMI) was calculated by dividing the individual's weight in kilograms by the square of the height in meters.[12] The levels of serum fasting glucose, hemoglobin A1c (HbA1c), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), total cholesterol, and total testosterone were analyzed. Venous blood samples were taken from the participants between 08:00 and 10:00 in the morning after a 12-hour fasting period. Laboratory tests were performed by using standard methods.

The average chronic glucose levels were measured as follows by using HbA1c:

Estimated chronic glucose levels (mg/dL)= [(28.7xHbA1c %)-46:7].[9] The A/C glycemic ratio was measured by dividing ABG at baseline and the estimated chronic glucose levels.

STATISTICAL ANALYSIS

The Number Cruncher Statistical System 2007 (NCSS; Kaysville, Utah, USA) program was used for the statistical analysis. The Kolomogrov-Smirnov test was used to analyze normality. The descriptive data were expressed with mean±standard deviation, median (interquartile range), numeric variables, frequency, and percentages. In the analysis of normally distributed variables, Student's t-test was applied to examine the differences between the normally distrubited quantitative data. The differences between the two independent groups were examined using the non-parametric Mann-Whitney U test for the non-normally distributed variables. A Pearson chi-square test was used to compare qualitative data; $p<0.05$ was considered statistically significant.

RESULTS

A total of 45 diabetic patients with ED and 59 diabetic controls without ED were included in the study.

TABLE 1: Demographic and laboratuary data of the whole study group.

		n %	Mean±SD	Median (interquartile range)
Age (years)			55±10	
Body mass index (kg/m^2)				27.92 (25.19-30.42)
Hypertension	No	41 (%39.4)		
	Yes	63 (%60.6)		
Smoking	Never	37 (%35.6)		
	Yes	39 (%37.5)		
	Quitter	28 (%26.9)		
Total testosterone (ng/dL)				4.75 (3.74-6.10)
Admission blood glucose (mg/dL)				174 (157-192)
HbA1c (%)				6.6 (6.1-7.1)
Acute/Chronic hyperglycemia ratio			1.22±0.28	
Estimated chronic glucose values (mg/dL)				141.66 (132.63-151.46)
Total cholesterol (mg/dL)				206 (186-222)
HDL-C (mg/dL)			42±10	
LDL-C (mg/dL)			123±30	

SD: Standard deviation; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol.

The demographic features and the disease characteristics of the study population are shown in Table 1. No significant differences were observed in terms of age or BMI values between the diabetic ED patients and the controls (p=0.846, p=0.898, respectively). Smoking habit and the presence of HT were similar in the two groups (p=0.58, p=0.085; respectively). The total testosterone levels were lower in the diabetic ED patients than in the non-ED diabetic patients. However, the difference was not statistically significant (4.49 ng/dL vs 4.80 ng/dL, respectively; p=0.093). When the lipid parameters were compared between the two groups, the total cholesterol and LDL-C levels showed no statistical differences between the two groups (p=0.235, p=0.478; respectively). The mean HDL-C levels were significantly lower in the diabetic ED patients compared to the controls (40±9 mg/dL vs. 44±10 mg/dL; respectively; p=0.030).

Although the levels of median ABG, the median-estimated chronic glucose levels, and the median A/C glycemic ratios were higher in the diabetic ED patients (183 mg/dL vs. 166 mg/dL; 141.12 mg/dL vs. 140.11 mg/dL; 1.28±0.23 vs. 1.18±0.32; respectively), no statistical differences were noted in terms of the levels of ABG, the estimated chronic glucose, or the A/C glycemic ratios between the two groups (p=0.014, p=0.846, p=0.054, respectively) (Table 2).

DISCUSSION

In the present study, the serum total testosterone levels and the serum HDL-C levels were lower in the diabetic ED patients than in the diabetic patients without ED; only the latter showed a statistical significance. The levels of median ABG, the mean estimated chronic glucose levels, and the the median A/C ratio were higher in the diabetic ED patients, with no statistical differences.

Male sexual function is often affected in DM. Diabetes was demonstrated to be significantly associated with all aspects of sexual function, which involve orgasmic, ejaculatory, and erectile functions, as well as desire/libido.[12] DM is a common medical condition causing complications in several systems in the later stages of the disease.[13] Microvascular complications, such as nephropathy, neuropathy, and retinopathy, may be prevented by glycemic control.[14] Neural and vascular dysfunction, impaired glucose metabolism, HT, decreased testosterone values, smoking, alcohol consumption, and sedentary life are reported to be the main risk factors of ED in patients with DM.[15] Hyperglycemia causes an increase in reactive oxidative damage, impaired cavernous relaxation, peripheral neuropathy, and endothelial harm.[15] Insulin resistance causes increase in oxidative stress

TABLE 2: Comparison of demographic and laboratory data of the patients in terms of the presence of erectile dysfunction.

		Erectyle Dysfunction (Absent) (n=45, %43.3)			Erectyle Dysfunction (Present) (n=59, %56.7)			
		n,%	Mean±SD	Median (interquartile range)	n,%	Mean±SD	Median (interquartile range)	p value
Age (years)			55±9			55±11		[a]0.846
Body mass index (kg/m^2)				27.61 (24.91-31.02)			28.91 (25.39-30.10)	[b]0.898
Hypertension	No	22 (%48.9)			19 (%32.2)			[c]0.085
	Yes	23 (%51.1)			40 (%67.8)			
Smoking	Never	18 (%40.0)			19 (%32.2)			[c]0.580
	Yes	17 (%37.8)			22 (%37.3)			
	Quitter	10 (%22.2)			18 (%30.5)			
Total testosterone (ng/dL)				4.80 (4.20-6.20)			4.49 (3.59-6.05)	[b]0.093
Admission blood glucose (mg/dL)				166 (147-184)			183 (162-196)	[b]0.014*
HbA1c (%)				6.6 (6.1-7)			6.6 (6.2-7)	[b]0.846
A/C Glycemic ratio			1.18±0.32			1.28±0.23		[a]0.054
Estimated chronic glucose values (mg/dL)				140.11 (129.63-151.33)			141.12 (130.50-150.46)	[b]0.846
Total cholesterol (mg/dL)			208 (201-219)			200 (183-222)		[b]0.235
HDL-C (mg/dL)			44±10				40±9	[a]0.030*
LDL-C (mg/dL)			126±31				121±30	[a]0.478

[a]Student t-test; [b]Mann-Whitney U test; [c]Pearson Chi-square test; *p<0.05; HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; A/C: Acute to chronic; SD: Standard deviation.

and inflammation in endothelium; as a result, nitric oxide (NO) use in tissues increases, free radicals and endothelial dysfunction are observed, and the synthesis and release of NO decrease.[16] As a result of insufficient knowledge in understanding the disease development, early diagnosis and prevention are difficult. Some authors have investigated serum biomarkers that could provide early diagnosis of ED in DM; however, none of them are reliable enough to be used in daily practice.[17]

Impaired glucose metabolism is a risk factor for the development of ED in diabetic males.[18] The A/C glycemic ratio, is a novel marker, assessed by division of ABG to the estimated average glucose (eAG). Here, eAG was measured by using HbA1c.[9] It is considered to be more reliable than the absolute hyperglycemia and HbA1c measurements.[19,20] The A/C glycemic ratio has been shown to be an important marker in "allcomer" patients who underwent percutaneous coronary intervention and in diabetic acute myocardial infarctus (AMI) patients.[10,21] It has also been demonstrated that the A/C glycemic ratio is a more reliable prognostic marker in adverse hospital events following AMI than ABG alone.[10] In this work, although the levels of the median A/C glycemic ratio were lower in the diabetic ED patients, no statistical differences were noted. We think that this result can be explained by the low sample size of the study and the patients generally having regulated DM.

HT, low testosterone levels, and smoking are reported to be risk factors of ED in patients with DM, and these factors have been evaluated in this study. Endothelial dysfunction is a shared pathogenesis both in HT and ED. However the association between HT and ED has not been clarified.[22] In this study, the presence of HT was similar in the two groups.

Smoking is a common addiction that is associated with several health problems.[23] Lifestyle changes, such as reducing smoking, physical activity, establishing a healthy diet, maintaining ideal BMI, and regulating blood glucose has been shown to reduce the risk of ED and metabolic syndrome.[24] Smoking is thought to cause sexual dysfunction through many paths. NO that is synthesized in the penil endothelium is the key mediator in vascular processes, including smooth muscle relaxation for the sexual acts. Smoking is known to cause a reduction in the synthesis of NO, leading to vaso-occlusive events in penis.[25] In the present study, no difference was ob-

served in terms of smoking between diabetics with and without ED.

Alterations in sex hormones is involved in the pathogenesis of sexual function.[26] Particularly, a low serum testosterone level is a well-known hormonal factor that plays a role in ED.[27] However, the results of the studies investigating the correlation of testosterone levels with ED remain controversial. Some reports have demonstrated an association between lower testosterone levels and ED, while some researchers have found no such relationship.[28,29] Although the diabetic patients in our study with ED had lower serum testosterone levels than the diabetic patients without ED, the difference was not statistically significant.

Although the exact mechanisms are unknown; vascular, neurogenic, hormonal, psychogenic, iatrogenic, and anatomic factors are thought to be involved in the pathogenensis of ED.[30] As mentioned above, atherosclerosis, endothelial dysfunction, and inflammation are the causes of vascular dysfunction leading to ED.[2] Among other factors, dislipidemia, which includes total cholesterol, triglyceride, LDL-C, and HDL-C, are responsible for atherosclerosis and endothelial dysfunction.[31] Although dyslipidemia is often observed in patients with type 2 DM, the underlying mechanism between these two disorders is not well established.[32] LDL-C is known as an important predictor of atherosclerosis and endothelial dysfunction, and decreasing the LDL-C level is the key approach in prevention and treatment of atherosclerosis.[31] Additionally, a low HDL-C level is also defined as an independent risk factor for CVD through endothelial dysfunction and atherosclerosis.[33] It has been hypothesized that lipid parameters may be related with ED. In a recent study, men with ED were shown to have increased systolic blood pressure, total cholesterol, and triglyceride levels.[34] In another study, it was reported that HDL and LDL/HDL were more significantly related to ED than other lipid parameters and were suggested as predictors of ED.[35] Our findings are consistent with the literature. The diabetic ED patients had significantly lower HDL-C levels than the diabetic patients without ED. Although it was not statistically significant, serum LDL-C levels were also higher in the diabetic ED patients than those without ED.

Nonetheless, this study has some limitations. First, it has a retrospective design with a small sample. Secondly, due to the design of the study, it was not possible to eliminate the confounding factors. Finally, another limitation is that the description of ED is based only on the IIEF.

CONCLUSION

ED may be the main presenting sign of subclinical atherosclerosis, CVD, and DM. Moreover, it has a great impact on individual's life quality. Since it is common in DM, we believe that developing biomarkers for the early diagnosis of ED will help to provide a treatment and improve the life quality of patients. Additionally, the early diagnosis of ED may be useful in providing some measure of control of the possible undiagnosed comorbidities. Although we could not find a statistically significant difference between the A/C glycemic ratio and ED in our study results, we think that well-designed prospective studies are needed in this area.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Emre Karabay;* ***Design:*** *Emre Karabay, Çağatay Tosun;* ***Control/Supervision:*** *Çağatay Tosun;* ***Data Collection and/or Processing:*** *Kemal Kayar;* ***Analysis and/or Interpretation:*** *Emre Karabay;* ***Literature Review:*** *Çağatay Tosun;* ***Writing the Article:*** *Emre Karabay;* ***Critical Review:*** *Çağatay Tosun.*

REFERENCES

1. Lewis RW, Fugl-Meyer KS, Corona G, Hayes RD, Laumann EO, Moreira ED Jr, et al. Definitions/epidemiology/risk factors for sexual dysfunction. J Sex Med. 2010;7(4 Pt 2):1598-607. [Crossref] [PubMed]
2. NIH Consensus Conference. Impotence. NIH consensus development panel on impotence. JAMA. 1993;270(1):83-90. [Crossref] [PubMed]
3. Kubin M, Wagner G, Fugl-Meyer AR. Epidemiology of erectile dysfunction. Int J Impot Res. 2003;15(1):63-71. [Crossref] [PubMed]
4. Shiri R, Hakama M, Häkkinen J, Tammela TL, Auvinen A, Koskimäki J. Relationship between smoking and erectile dysfunction. Int J Impot Res. 2005;17(2):164-9. [Crossref] [PubMed]
5. Selvin E, Burnett AL, Platz EA. Prevalence and risk factors for erectile dysfunction in the US. Am J Med. 2007;120(2):151-7. [Crossref] [PubMed]
6. Sáenz de Tejada I, Anglin G, Knight JR, Emmick JT. Effects of tadalafil on erectile dysfunction in men with diabetes. Diabetes Care. 2002;25(12):2159-64. [Crossref] [PubMed]
7. Oyelade BO, Jemilohun AC, Aderibigbe SA. Prevalence of erectile dysfunction and possible risk factors among men of South-Western Nigeria: a population based study. Pan Afr Med J. 2016;24:124. [PubMed] [PMC]
8. Al-Hunayan A, Al-Mutar M, Kehinde EO, Thalib L, Al-Ghorory M. The prevalence and predictors of erectile dysfunction in men with newly diagnosed with type 2 diabetes mellitus. BJU Int. 2007;99(1):130-4. [Crossref] [PubMed]
9. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ; A1c-Derived Average Glucose Study Group. Translating the A1C assay into estimated average glucose values. Diabetes Care. 2008;31(8):1473-8. Erratum in: Diabetes Care. 2009;32(1):207. [Crossref] [PubMed] [PMC]
10. Marenzi G, Cosentino N, Milazzo V, De Metrio M, Cecere M, Mosca S, et al. Prognostic value of the acute-to-chronic glycemic ratio at admission in acute myocardial infarction: a prospective study. Diabetes Care. 2018;41(4):847-53. [Crossref] [PubMed]
11. Akkus E, Kadioglu A, Esen A, Doran S, Ergen A, Anafarta K, et al; Turkish Erectile Dysfunction Prevalence Study Group. Prevalence and correlates of erectile dysfunction in Turkey: a population-based study. Eur Urol. 2002;41(3):298-304. [Crossref] [PubMed]
12. Burke JP, Jacobson DJ, McGree ME, Nehra A, Roberts RO, Girman CJ, et al. Diabetes and sexual dysfunction: results from the Olmsted County study of urinary symptoms and health status among men. J Urol. 2007;177(4):1438-42. [Crossref] [PubMed]
13. Centers for Disease Control and Prevention. National diabetes statistics report: estimates of diabetes and its burden in the United States, 2014. Atlanta: Centers for Disease Control and Prevention; 2014. [Link]
14. Fullerton B, Jeitler K, Seitz M, Horvath K, Berghold A, Siebenhofer A. Intensive glucose control versus conventional glucose control for type 1 diabetes mellitus. Cochrane Database Syst Rev. 2014;2014(2):CD009122. [Crossref] [PubMed] [PMC]
15. Morano S. Pathophysiology of diabetic sexual dysfunction. J Endocrinol Invest. 2003;26(3 Suppl):65-9. [PubMed]
16. Cersosimo E, DeFronzo RA. Insulin resistance and endothelial dysfunction: the road map to cardiovascular diseases. Diabetes Metab Res Rev. 2006;22(6):423-36. [Crossref] [PubMed]
17. Patel DP, Craig JR Jr, Myers JB, Brant WO, Hotaling JM. Serum biomarkers of erectile dysfunction in diabetes mellitus: a systematic review of current literature. Sex Med Rev. 2017;5(3):339-48. [Crossref] [PubMed]
18. Binmoammar TA, Hassounah S, Alsaad S, Rawaf S, Majeed A. The impact of poor glycaemic control on the prevalence of erectile dysfunction in men with type 2 diabetes mellitus: a systematic review. JRSM Open. 2016;7(3):2054270415622602. [Crossref] [PubMed] [PMC]
19. Roberts GW, Quinn SJ, Valentine N, Alhawassi T, O'Dea H, Stranks SN, et al. Relative hyperglycemia, a marker of critical illness: introducing the stress hyperglycemia ratio. J Clin Endocrinol Metab. 2015;100(12):4490-7. [Crossref] [PubMed]
20. Su YW, Hsu CY, Guo YW, Chen HS. Usefulness of the plasma glucose concentration-to-HbA1c ratio in predicting clinical outcomes during acute illness with extreme hyperglycaemia. Diabetes Metab. 2017;43(1):40-7. [Crossref] [PubMed]
21. Lee TF, Burt MG, Heilbronn LK, Mangoni AA, Wong VW, McLean M, et al. Relative hyperglycemia is associated with complications following an acute myocardial infarction: a post-hoc analysis of HI-5 data. Cardiovasc Diabetol. 2017;16(1):157. [Crossref] [PubMed] [PMC]
22. Braun M, Wassmer G, Klotz T, Reifenrath B, Mathers M, Engelmann U. Epidemiology of erectile dysfunction: results of the 'Cologne Male Survey'. Int J Impot Res. 2000;12(6):305-11. [Crossref] [PubMed]
23. Shiverick KT, Salafia C. Cigarette smoking and pregnancy I: ovarian, uterine and placental effects. Placenta. 1999;20(4):265-72. [Crossref] [PubMed]
24. Giugliano D, Giugliano F, Esposito K. Sexual dysfunction and the Mediterranean diet. Public Health Nutr. 2006;9(8A):1118-20. [Crossref] [PubMed]
25. McMahon CG, Touma K. Predictive value of patient history and correlation of nocturnal penile tumescence, colour duplex Doppler ultrasonography and dynamic cavernosometry and cavernosography in the evaluation of erectile dysfunction. Int J Impot Res. 1999;11(1):47-51. [Crossref] [PubMed]
26. Hatzimouratidis K, Amar E, Eardley I, Giuliano F, Hatzichristou D, Montorsi F, et al; European Association of Urology. Guidelines on male sexual dysfunction: erectile dysfunction and premature ejaculation. Eur Urol. 2010;57(5):804-14. [Crossref] [PubMed]
27. Martínez-Jabaloyas JM, Queipo-Zaragozá A, Pastor-Hernández F, Gil-Salom M, Chuan-Nuez P. Testosterone levels in men with erectile dysfunction. BJU Int. 2006;97(6):1278-83. [Crossref] [PubMed]
28. Rastrelli G, Corona G, Maggi M. Testosterone and sexual function in men. Maturitas. 2018;112:46-52. [Crossref] [PubMed]
29. Rhoden EL, Telöken C, Sogari PR, Souto CA. The relationship of serum testosterone to erectile function in normal aging men. J Urol. 2002;167(4):1745-8. [Crossref] [PubMed]
30. Chew KK, Bremner A, Stuckey B, Earle C, Jamrozik K. Is the relationship between cigarette smoking and male erectile dysfunction independent of cardiovascular disease? Findings from a population-based cross-sectional study. J Sex Med. 2009;6(1):222-23. [Crossref] [PubMed]
31. Authors/Task Force Members:, Catapano AL, Graham I, De Backer G, Wiklund O, Chapman MJ, Drexel H, et al. 2016 ESC/EAS guidelines for the management of dyslipidaemias: the task force for the management of dyslipidaemias of the european society of cardiology (ESC) and european atherosclerosis society (EAS) developed with the special contribution of the european assocciation for cardiovascular prevention & rehabilitation (EACPR). Atherosclerosis. 2016;253:281-344. [PubMed]
32. Vergès B. Pathophysiology of diabetic dyslipidaemia: where are we? Diabetologia. 2015;58(5):886-99. [Crossref] [PubMed] [PMC]
33. Rader DJ, Hovingh GK. HDL and cardiovascular disease. Lancet. 2014;384(9943):618-25. [Crossref] [PubMed]
34. Yao F, Huang Y, Zhang Y, Dong Y, Ma H, Deng C, et al. Subclinical endothelial dysfunction and low-grade inflammation play roles in the development of erectile dysfunction in young men with low risk of coronary heart disease. Int J Androl. 2012;35(5):653-9. [Crossref] [PubMed]
35. Li M, Ma Z, Zhang XL, Guo LQ, Yuan MZ. Significance of blood lipid parameters as effective markers for arteriogenic erectile dysfunction. Andrology. 2020;8(5):1086-94. [Crossref] [PubMed]