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Lifestyle changes for improving ED
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·*Review*·

Do lifestyle changes work for improving erectile dysfunction?

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Abstract

The main cause of erectile dysfunction (ED) is organic in nature, with vascular etiologies being the most common risk factors. Although there have been sufficient data on the relationship between ED and several well-recognized risk factors, including aging, coronary artery disease, atherosclerosis, diabetes mellitus, dyslipidemia, high blood pressure, and pelvic surgeries, little attention has been paid by the urologists to the role of lifestyle factors in ED. However, accumulating data from basic science and clinical studies have determined a link between the occurrence of ED and a number of lifestyle factors, such as smoking, obesity, alcohol consumption, and lack of physical activity. The application of findings from animal and human studies to the clinical practice regarding the modification of lifestyle factors could help improving ED as well as reducing the risks of developing cardiovascular diseases. This communication addresses the impact of lifestyle factors on erectile function and the potential benefits of modifying these factors to improve ED in respect to the current evidence. *(Asian J Androl 2008 Jan; 10: 28–35)*

Keywords: erectile dysfunction; lifestyle; smoking; obesity; alcohol; sedentary life

1 Introduction

Erectile function is a complex phenomenon regulated by neural, hormonal, vascular and structural factors. Penile erection is the end result of a chain of events that cause smooth muscle relaxation in the corpora cavernosa of the penis. Upon sexual stimulation, nitric oxide (NO), the key mediator for the initiation and maintenance of penile erection, is synthesized and released by the autonomic nerves and endothelium, serving the penile arteries and nerve terminals of the corpus cavernosum [1]. NO enters the cavernosal smooth muscle cell and activates soluble guanylate cyclase (sGC), which promotes the formation of cyclic guanosine monophosphate (cGMP). Through a cascade of events, cGMP reduces intracellular calcium levels, allowing for relaxation of smooth muscle cells of the vasculature. Good erectile function depends on a delicate homeostasis between vascular constricting and relaxing factors through a healthy endothelium.

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The vascular endothelium of the penis plays a pivotal role in modulating vascular tone and blood flow into the penis in response to humoral, neural, and mechanical stimuli. In endothelial dysfunction, the regulatory role of the endothelium is hindered, resulting in decreased responsiveness to vasodilatory mediators and/or increased sensitivity to various vasoconstricting agents. Well-recognized disease states and vascular risk factors, such as diabetes mellitus, coronary artery disease, atherosclerosis, hypertension, and smoking, have long been known to impair penile endothelial function, resulting in a decrease in endothelial-dependent corpora cavernosal smooth muscle relaxation through decreased expression and activity of neuronal and endothelial NO synthase (nNOS and eNOS), impaired NO release, and/or increased destruction or total loss of NO bioactivity in the penis [2].

Although the impact of abovementioned well-known risk factors and disease states on erectile function have been extensively elucidated, little attention has been paid by the sexual medicine specialists to the role of lifestyle factors in penile endothelial function and ED. As ED has a significant impact on quality-of-life by reducing self-esteem and confidence, and by affecting interpersonal relationships to the point of termination, all aspects of the contributing factors need to be evaluated. Recently

accumulating evidences from basic science and clinical studies have demonstrated the link between the occurrence of ED and a number of lifestyle factors, such as smoking, obesity, alcohol consumption, and lack of physical activity (Figure 1) [3, 4]. More importantly, as ED and cardiovascular diseases have epidemiologic and pathophysiologic associations, it is crucial to ascertain these unfavorable lifestyle factors not only for erectile function but also for a generalized endothelial function.

Current practice in ED treatment has been mainly based on utilizing type 5 phosphodiesterase inhibitors (PDE-5i) as the first-line approach for majority of cases, because of their high efficacy, ease of use, and acceptable safety profile. However, some ED patients may not be eligible for PDE-5i due to a number of factors, including lack of efficacy, side effects, contraindications, loss of efficacy, advanced age, progression of the underlying disease, and uncontrolled co-morbidities [5]. Recent evidence from clinical studies suggests that the modification of lifestyle factors could help improving ED as well as reducing the risks of developing cardiovascular disease. Therefore, this communication addresses the impact of lifestyle factors on erectile function and the potential benefits of modifying these factors to improve ED in respect to the current evidence.

2 Smoking

Although there is much discussion regarding the role of smoking on erectile function, most investigators still consider smoking as a risk factor for vasculogenic ED [6]. However, the underlying pathophysiology of ED in smokers remains poorly understood.

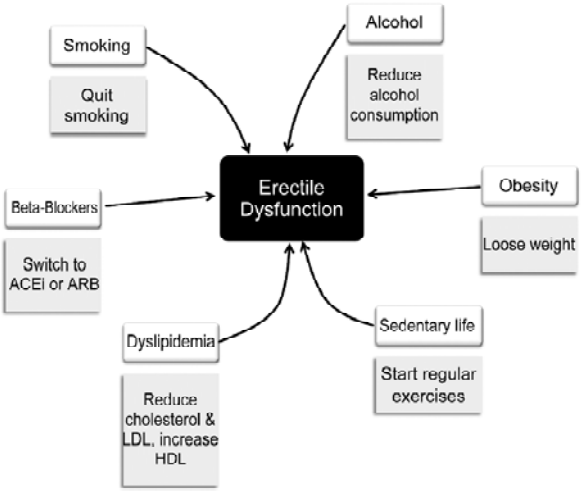

Figure 1. Effects of lifestyle factors on erectile function and beneficial behaviors for improving erectile dysfunction (ED). ACEi, Angiotensin-converting enzyme inhibitors; ARB, Angiotensin-receptor blockers; HDL, High-density lipoproteins; LDL, Low-density lipoprotein.

In Massachusetts Male Aging Study (MMAS), Feldman *et al.* [7] found that smokers were more likely to have ED than nonsmokers (24% *vs*. 14%, adjusted odds ratio [OR], 1.97). Controlling for multiple confounders, Mannino *et al.* [8] investigated whether cigarette smoking was associated with ED among middle-aged men using a secondary analysis of a cross-sectional survey of 4 462 US Army veterans from the Vietnam era. The study sample consisted of 1 162 nonsmokers, 1 292 former smokers, and 2 008 current smokers. The prevalence of ED was found to be 2.2% among nonsmokers, 2.0% in former smokers, and 3.7% in current smokers (P = 0.005). The unadjusted OR of the association between smoking and reported ED was 1.8. They also demonstrated that neither the number years of smoking nor the number of cigarettes smoked daily were significant predictors of ED in current smokers. After adjusting various risk factors, including age, vascular disease, psychiatric disorders, hormonal factors, substance abuse, marital status, and race, the authors concluded that a higher percentage of cigarette smokers reported ED than did nonsmokers.

Others have also demonstrated that the duration of smoking, the number of cigarettes smoked per day, and the number of years smoking directly correlated with ED [9]. The results of this study demonstrated not only a higher prevalence, but also heightened severity of ED. Clinically, there are strong parallels and shared risks among smoking, coronary artery disease, atherosclerosis and ED. Basic science studies provide strong indirect evidence that smoking may affect penile erection by the impairment of endothelium-dependent smooth muscle relaxation. To establish a causal explanation, dose response is one of the key components. Feldman *et al.* [7] presented data of a gradient by showing the sequentially increasing risk of ED in smokers with no exposure to passive smoke, those with passive exposure only at home, those with passive exposure at work and those with passive exposure at both places. The adjusted ED incidences were 14%, 23%, 28% and 33%, respectively [7]. Other researchers analyzed the role of smoking as a risk factor for ED using data from a cross-sectional cohort in the general population [10]. In this study by Mirone *et al.* [10], a total of 2 010 men older than 18 years were randomly identified and interviewed by 143 general practitioners. In comparison with nonsmokers, current smokers had an OR of ED of 1.7 and ex-smokers of 1.6 of developing ED. Of interest, they noted a true association between smoking and ED risk in subjects without any history of cardiovascular disease, cardiomyopathy, hypertension, diabetes or neuropathy. These researchers provide evidence that smoking influences the risk of ED and the duration of the habit increased the risk.

A significant dose response relationship of smoking and cavernous arterial occlusion was reported by Rosen *et al.* [11]. More recent studies supporting the evidence revealed that cumulative smoking in pack-years suggests a dose response pattern with the risk of ED [12] and as in Boston Area Community Health (BACH) survey this dose response association between smoking and ED is significant with more than 20 pack-years of exposure [13]. Passive smoking remains unclear whether it causes ED or not. In MMAS [7], passive exposure to cigarette smoke predicted ED, whereas in the BACH survey, the risk of ED was slightly but not significantly increased [13].

In addition to epidemiological studies, clinical and animal studies support the concept that smoking causes peripheral vascular disease and adversely affects erectile function by impairing endothelium-dependent smooth muscle relaxation [14]. In one study, researchers reviewed angiograms of the hypogastric-cavernous arterial bed in young men with ED who had been referred for selective pudendal angiography [11]. Patients with ≥ 50% luminal diameter reduction were found to have smoked more pack-years than patients without arterial disease. This study showed that cigarette smoking was an independent risk factor for the development of atherosclerotic lesions of the internal pudendal arteries of young, impotent men. Using a polysomnographic assessment, Hirshkowitz *et al.* [15] examined the relationship between cigarette smoking and erectile physiology in 314 men with ED. The authors observed that penile rigidity during nocturnal erections inversely correlated with the number of cigarettes smoked per day and hypothesized that smoking was associated with impairment of autonomic function and measures of intracorporeal pressures. The group of men who smoked the most (more than 40 cigarettes per day) had the shortest duration of nocturnal tumescence and quickest period for detumescence. Short-term studies have demonstrated that impaired nocturnal tumescence recording could be reversed by an abrupt cessation of smoking [16].

While it is known that chronic smoking damages the endothelium, nicotine can acutely cause significant vasospasm of the penile arteries [17]. Juenemann *et al.* [18] assessed the effects of 7 to 12 minutes of acute smoke exposure on penile erection in dogs. After inhalation of cigarette smoke, five of six did not achieve erection with neurostimulation. Arterial inflow and veno-occlusion were impaired with almost complete abolition of venous restriction. Moreover, chronic smoking has been documented to be associated with ultrastructural damage to the corpora cavernosa and to decrease cavernous NOS levels [19]. Other animal studies have shown ultrastructural, enzymatic and morphological changes in the endothelium of smoke-exposed animals [20, 21]. The effects are illustrated in Figure 2. Free radicals and aromatic compounds decrease the endothelial synthesis of NO, causing impaired endothelium-dependent relaxation of arteries, which is the earliest clinical sign of endothelial dysfunction [22]. The impaired endothelium-dependent relaxation of saphenous vein rings appears to be caused by decreased activity of eNOS, which is attributable to an inadequate supply of the coenzyme tetrahydrobiopterin [23]. Cigarette smoke extracts can cause smooth muscle contraction by the superoxide anion-mediated degradation of NO [24].

Reversal of ED by cessation of smoking may work for treatment without medications or when medications fail. Supporting data from Mannino *et al.* [8] revealed that former smokers have significantly low rate of ED compared to current smokers (2% *vs.* 3.7%). In a prospective study, Guay *et al.* [16] reported significant and rapid improvement in penile tumescence and rigidity after cessation of smoking in patients smoking over 30 packs-year. Contrary to these, in the Health Professionals Follow-up Study (HPFS) [3] including 22 086 men revealed, although there remains a small difference, current and past smokers had a significant increased risk of ED (current smokers' relative risk [RR]: 1.5; 95% CI: 1.3–1.7; past smokers' RR: 1.2, 95% CI, 1.1–1.3). Additionally, Derby *et al.* [25] reported reassessment of the MMAS population regarding the modifiable risk factors. By design, the analysis sample excluded men with baseline ED, diabetes, heart disease and prostate cancer, which are medical diseases or treatments that may overwhelm any association of smoking with ED. However, in this 8-year analysis, 50% of smokers stopped

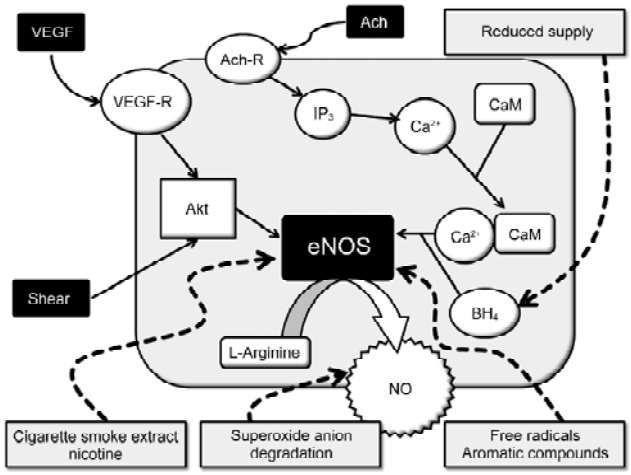

Figure 2. The effects of smoking on endothelium. eNOS, endothelial nitric oxide synthase; NO, nitric oxide; Ach, acetylcholine; Ach-R, Ach receptor; VEGF, vascular endothelial growth factor; VEGF-R, VEGF receptor; IP, inositol triphosphate; CaM,calmodulin; Akt, serine/threonine kinase; BH_4, tetrahydrobiopterin. Adapted from McVary *et al.* [14].

smoking; nevertheless, no status change in ED was observed among the quitters. Thus, smoking cessation in middle-aged men did not significantly decrease the risk of ED. Therefore, risk factors for ED may require earlier intervention or a prolonged period for reversal, similar to that in the differences in reversibility in coronary artery disease and death from myocardial infarction.

3 Obesity and dyslipidemia

High low-density lipoprotein (LDL) and total cholesterol, and low high-density lipoprotein (HDL) cholesterol are known risk factors for vascular disease. Because of higher saturated fats in diets and sedentary lifestyle, the prevalence of obesity is increasing in the modern world. Population-based studies demonstrate that dyslipidemia and obesity are major risk factors for ED. Among men with ED, 26% were found to have elevated serum cholesterol levels [26]. Recent studies have shown that the prevalence of hypertension and hyperlipidemia in ED patients being between 40%–80% [27].

In the original MMAS study, having any degree of ED was not dependent upon the body mass index (BMI), but the probability of having ED was inversely related to the HDL levels. The moderate and complete ED rates were 25% and 16%, respectively, for the High-density lipoproteins (HDL) levels of 30 mg/dL, while it was 7% and 0% for the moderate and complete ED, respectively, when the HDL levels were considered to be 90 mg/dL [28]. In 1994, Wei *et al.* [29] reported the OR of developing ED for every mmol/L increase in cholesterol was 1.32 (95% CI, 1.04–1.68), while every mmol/L of increase in HDL cholesterol was associated with 0.38 times increased risk for ED (95% CI, 0.18–0.80). This article supports the MMAS data regarding the importance of the HDL cholesterol. In addition to the longitudinal population-based studies, Chung *et al.* [30] investigated 325 men who were diagnosed with ED regarding the effect of intracavernosal injections on the erectile response as graded on a scale from 0 to 4 [30]. They showed significantly better mean erectile responses in patients with > 120% ideal body weight than in < 120% ideal body weight (1.62 *vs.* 1.32) after intracavernosal injections.

Using a nationally representative managed care database claims that covered 51 health plans with 28 million lives between 1995 and 2002, Seftel *et al.* [27] found that 42.4% of men with ED had hyperlipidemia. This rate is 5.4% higher than the rate in the study of Solomon *et al.* [31] for hyperlipidemia. The Rancho Bernardo Study assessed age, smoking, hypertension, diabetes, hypercholesterolemia and obesity in 1 810 men from 1972 to 1974, and 25 years later 570 surviving males completed the International Index of Erectile Function (IIEF-5) questionnaire. In a cumulative logit model, age, hypercholesterolemia and obesity were found to be independent predictors of increased ED severity [32]. Roumeguere *et al.* [33] demonstrated the prevalence of hypercholesterolemia as 70.6% in 216 ED patients, whereas this value was only 52% in controls with normal erectile function. In another case-control study by Nikoobakht *et al.* [34], mean plasma cholesterol and low-density lipoprotein (LDL) levels in individuals suffering from ED were significantly higher than controls. However, no difference in the mean plasma triglyceride and HDL levels was reported [34]. In the health professionals follow-up study (HPFS) [35], BMI > 28.7 kg/m^2 remained independently associated with ED (RR, 1.2; 95% CI, 1.0–1.5). One drawback of this study was that assessment of ED was based on a single question. Blanker *et al.* [36] demonstrated that BMI > 30 kg/m^2 was associated with ED on univariate and multivariate analyses (OR, 3.0, 95% CI, 1.7–5.4). Unfortunately this study did not include important factors such as hypertension and diabetes on multivariate analysis.

The association between hyperlipidemia and ED was originally attributed to atherosclerosis in the hypogastric-cavernosal arterial vascular bed, resulting in a decline in penile blood flow. Impairment of endothelium-dependent relaxation in various vascular beds of men with hypercholesterolemia has been well established [37, 38]. Several researchers have attempted to locate biochemical mediators that reverse the endothelial effects of hyperlipidemia, which interferes with cavernous smooth muscle relaxation. Oxidized LDL (ox-LDL) is found in plaque formation to the endothelium and is a major cause of impaired relaxation [39]. Ox-LDL, the production of superoxide radicals, and functional impairment of eNOS are postulated to be the prime mechanisms for the development of ED in the early stages of hyperlipidemia [40–42]. Endothelin-1 has also been demonstrated to be increased in hyperlipidemic patients, although the exact mechanism of activation has not been fully elucidated [43].

In an animal model, Gholami *et al.* [44] revealed that hypercholesterolemic rats had lower nerve content, fewer endothelial cells, and higher smooth muscle content than rats maintained with normal cholesterol levels. In this study, rats placed on high-cholesterol diets showed hypermyelination, severe atrophy of axons, a decrease in the number and size of non-myelinated axons, disarray of the smooth muscle cells with scant myofilaments and foamy cytoplasm, and denuded endothelial lining of the sinusoids covered by numerous platelets. The authors concluded that a high-fat diet caused ED with accompanying neurological and vascular changes, and theorized that a vascular endothelial growth factor (VEGF) and adeno-associated virus-mediated brain-derived nerve growth factor (AAV-BDNF) could reverse some of the underlying vascular pathology in hypercholesterolemia.

In another animal study, intracavernous injections of VEGF were noted to protect the corporal endothelium from hypercholesterolemia-induced injury, thus preserving endothelial-dependent corporal smooth muscle relaxation in the hypercholesterolemic rabbit [45].

In histological evaluations, Juenemann *et al*. [46] demonstrated significant cavernous smooth muscle cell degeneration with a loss of intercellular contacts in rabbits put on high-cholesterol diets. Their data imply that impaired lipid metabolism causes cavernous smooth muscle degeneration, which plays a major role in the pathogenesis of ED. Ox-LDL, a thromboxane A2 receptor antagonist, produced a protective metabolic effect on the erectile tissue of these hypercholesterolemic rabbits. This is another avenue of therapy worthy of clinical exploration.

Clinical studies performed in ED men contributed what was found in the animal studies. Atahan *et al*. [47] evaluated the relationship between the lipid levels and electromyography of the corpora cavernosa (CC-EMG) in 39 patients with ED following intracavernous papaverine injections. The authors demonstrated a correlation between the presence of vasculogenic ED and the cholesterol levels. On CC-EMG, there was a significant difference in pre- and post-injection amplitudes between those patients with vasculogenic and non-vasculogenic ED.

Although the effect of lipid-lowering drugs on erectile function remains undefined at this stage, recent evidence supports the benefit of using lipid-lowering approaches. Saltzman *et al*. [48] studied the use of statins to lower cholesterol and improve erectile function in men who had hypercholesterolemia as the only risk factor for ED. These investigators found that eight of the nine men in the study reported improved erections adequate for sexual intercourse as measured by nocturnal penile tumescence and rigidity (Rigiscan) testing after using atorvastatin with a mean 3.7 months of treatment. They found a significant decrease in mean total and LDL cholesterol after treatment and showed an increase in erectile-function-domain scores from 14.2 to 20.7 as measured by the Sexual Health Inventory of Male (SHIM) questionnaire. Objective measurement using RigiScan showed an increase in mean penile rigidity at both the base and tip. The authors concluded that erectile function improved in men with hypercholesterolemia as the only risk factor for ED when treated with atorvastatin.

Additionally, in a case-control study, contrary to Derby *et al*. [25], loosing weight was proven to be independently associated with changes in the IIEF scores. Esposito *et al*. [4] carried out a randomized clinical trial of 110 obese ED men who did not have diabetes, hypertension, or hyperlipidemia. Men in the intervention group received detailed advice regarding loosing 10% or more of their total body weight by reducing caloric intake and increasing physical activity, while men in the control group were given general information about healthy food choices and exercise. These investigators demonstrated significantly decreased BMI and increased mean IIEF scores in the intervention group within 2 years.

Finally, as both obesity and dyslipidemia promote atherosclerosis, which are independent risks for development of ED, a detailed analysis of these conditions are crucial in clinical settings. A number of studies showing evidence for the link among obesity and/or dyslipidemia and ED is summarized in Tables 1 and 2.

4 Alcohol consumption

Excess alcohol consumption has long been regarded as a risk factor for ED. Although it is considered to improve erection and sexual drive when utilized small amounts because of its vasodilatory effect and suppression of anxiety, large amounts can cause central sedation, decreased libido and ED [49].

In MMAS, the adjusted incidence for ED was 16% in men with < 1 drink/day, 16% in those with 1–3 drinks/day and 15% in those with more than 4 drinks/day [7]. This incidence was adjusted for age, smoking, cholesterol, hypertension, physical activity, fat intake, and obesity, testosterone, depression and antihypertensive medications. In the cross-sectional HPFS study, the multivariate adjusted RRs for ED were decreased with moderate levels of alcohol consumption. The RRs were 1.0, 0.9, 0.8 and 1.0 for 0.1–4.9, 5.0–14.9, 15–29.9, > 30 g/day of alcohol consumption, respectively [35]. In the HPFS prospective cohort study, no significant difference in the risk of developing ED was found in all categories of alcohol consumption. The multivariate RRs for 0.1–4.9, 5.0–14.9, 15.0–29.9 and > 30 g/day of alcohol was 1.0, 1.0, 1.0 and 1.1 [3]. However, Derby *et al*. [25] prospectively evaluated the effect of alcohol consumption on erectile function and were unable to find any relationship between heavy drinking and ED. Similar results were observed in the study by Paick *et al*. [50]. In contrast, Polsky *et al*. [12] reported a significantly higher OR with > 8 drinks/day than 1–7 drinks/day (2.09 *vs*. 1.96) after adjusting age, the education levels, presence of diabetes and smoking

Interestingly, a recent meta-analysis which included 11 cross-sectional studies found that regular alcohol consumption was negatively correlated with ED (OR, 0.79; 99% CI, 0.67–0.92) [51]. Although any association was observed between less alcohol consumption (1–7 drinks/week) and ED, the authors reported that consumption of 8 or more drinks/week significantly reduced the risk of ED (OR, 0.85; 99% CI, 0.73–0.99). These contradictory results from epidemiological studies are not sufficient to make a conclusion regarding the role of al-

Table 1. Major studies representing the association between dyslipidemia and erectile dysfunction (ED). LDL, Low-density lipoproteins; HDL, high-density lipoproteins.

Study	Year	Patient number	Findings
Nikoobakht *et al.* [34]	2005	100 cases, 100 controls	ED patients have higher cholesterol and LDL levels.
Fung *et al.* [32]	2004	570 cases	Hyperlipidemia is associated with ED after a 25-year-follow-up.
Seftel *et al.* [27]	2004	27 cases, 2 325 controls	42% of men with ED have hyperlipidemia.
Roumeguere *et al.* [33]	2003	215 cases, 100 controls	Prevalence of hypercholesterolemia is 70.6% *vs.* 52% in ED and non-ED men.
Solomon *et al.* [31]	2003	174 cases	37% of men with ED have hyperlipidemia.
Atahan *et al.* [47]	1997	39 cases	There is a correlation between vasculogenic ED and cholesterol levels.
Wei *et al.* [29]	1994	3 250 cases	There is an inverse correlation between ED and HDL levels.
Feldman *et al.* [28]	1994	1 709 cases	Higher HDL levels are negatively correlated with the presence of ED.

Table 2. Studies demonstrating clinical evidence between obesity and erectile dysfunction (ED). IIEF, international index of erectile function; BMI, body mass index.

Study	Year	Patient number	Findings
Esposito *et al.* [4]	2004	110 cases	Decrease in BMI is associated with an increase in the IIEF scores.
Fung *et al.* [32]	2004	570 cases	Obesity is not associated with ED after a 25-year-follow-up.
Bacon *et al.* [35]	2003	31 742 cases	A BMI of >28.7 is associated with ED.
Blanker *et al.* [36]	2001	1 688 cases	Obesity is associated with ED.
Derby *et al.* [25]	2000	593 cases	Baseline obesity predicts a higher risk for ED.
Chung *et al.* [30]	1999	325 cases	The relation between obesity and ED is dependent on vascular risk factors.

cohol consumption in ED. Therefore, further basic science and clinical research is needed by evaluating the amount, the duration and the type of alcohol consumed in order to delineate whether alcohol is a contributor or protector for ED.

5 Physical activity

Given the similar risk factor profiles for ED and cardiovascular diseases, it can be hypothesized that they may share similar protective factors including physical activity. Recently, there have been explosion of data regarding the benefit of physical activity on erectile and cardiovascular function. In a number of independent cross-sectional and cohort studies, regular exercise has been shown to be beneficial on erectile function.

In MMAS [7], the adjusted incidence of ED was found to be lower in those with > 200 kcal/day of physical activity compared to those with < 200 kcal/day of physical activity (15% *vs.* 19%). Another supporting data from Derby *et al.* [25] clearly demonstrated the reduced risk of ED in men with a sedentary lifestyle at baseline when they became physically active during the course of the study. Men who initiated physical activity in midlife had a 70% reduced risk for ED relative to those who remained sedentary. The highest risk for ED was among men who were sedentary both at the baseline visit and follow-up. In this study, reduction in smoking, obesity and the amount of alcohol consumption were also found to be associated with a lower overall incidence of ED, although not as strongly as the levels of physical activity.

Other cross-sectional studies have also shown significantly reduced rate of ED when higher levels of physical activity were employed. In HPFS [35], physical activity was associated with lower risk for ED; the multivariate relative risk was 0.7 (95% CI, 0.6–0.7) for > 32.6 metabolic equivalent hours of exercise per week *vs.* 0 to 2.7 metabolic equivalent hours of exercise per week. In 2006, Bacon *et al.* [3] investigated the impact of health behaviors on development of ED among 22 086 participants. They found that 3 905 men reported occurrences of ED within 14-year-follow-up period. These investigators reported that higher levels of physical activity were associated with a reduced risk of ED. They also found that higher levels of sedentary behavior were a positive predictor for ED.

Nicolosi *et al.* [52] conducted a study in 2 412 men aged 40 to 70 in Brazil, Italy, Japan and Malaysia to examine the relationship between the lifestyle factors and ED. Of these men, 1 335 had no diagnosis of cardiovascular or prostate diseases, diabetes, ulcer or depression.

They demonstrated an inverse correlation between ED and the levels of physical activity. Among study participants, 13.9% of men with greater than average levels of physical activity had ED, while 17.5% of men with average levels of physical activity demonstrated ED; this rate was 31.8% in men with less than average physical activity. In a multivariate regression analysis, Esposito *et al.* [4] showed that physical activity as well as BMI and C-reactive proteins independently predicted the IIEF scores.

A recent meta-analysis by Cheng *et al.* [53] including 7 cross-sectional studies evaluated the impact of physical activity on erectile function. The analysis revealed that the presence of ED was negatively associated with physical activity. These investigators reported a dose response relationship between ED and physical activity, with higher physical activity conferring lower risks for ED (OR = 1 for low activity, OR = 0.63 for moderate activity and OR = 0.42 for high activity). They concluded that, although causality cannot be demonstrated from cross-sectional studies, the apparent protective effect of physical activity on ED should be further investigated using large-scale cohort studies or randomized controlled trials.

6 Others

Many men with ED have underlying vascular risk factors, such as diabetes, hypertension, coronary artery disease, smoking, and lipid abnormalities. Controlling these risk factors with lifestyle changes and/or proper medications may improve the chance of success with available ED treatments [54]. ED patients taking medications known to have adverse sexual side effects can be switched to an alternative drug or drug class when appropriate. For example, patients who are taking propranolol or metoprolol, which are known to aggravate sexual dysfunction, might be changed to atenolol, while patients receiving anti-hypertensive medications may substitute another class of drug altogether, such as angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin-receptor blockers (ARBs). Losartan (an angiotensin II receptor antagonist), in particular, has been shown to have a beneficial effect on erectile function [55]. Similarly, antidepressive medications known to worsen erectile function can be switched those with less or no deleterious effects on erectile function. Controlling blood sugar with diet and antidiabetic medications may also help improve erectile and vascular endothelial function.

7 Conclusion

Clinical studies provide evidence that an organic etiology is responsible for more than 80% of patients with ED. Although there have been sufficient data on the relationship between ED and several well-recognized risk factors, including aging, coronary artery disease, atherosclerosis, diabetes mellitus, high blood pressure, and pelvic surgeries, less attention has been paid by the sexual medicine specialists to the role of the lifestyle factors in ED. Recent basic science and clinical studies have determined a link between the occurrence of ED and a number of lifestyle factors, such as smoking, obesity, alcohol consumption, and lack of physical activity. Efforts focusing on the modification of these lifestyle factors could help improving ED, as well as reducing the risks of developing cardiovascular disease. Further research is needed to elucidate the exact pathophysiology of these lifestyle factors on erectile function and potential benefits of modifying these unfavorable risk factors on improving erectile function.

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