Physical activity and erectile dysfunction in middle-aged men: a brief review

Running title: physical activity and ED in middle-aged men

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ABSTRACT
The prevalence of erectile dysfunction is high in men of all ages and increases greatly in the elderly. In particular severity and prevalence both increase with aging. Since erectile dysfunction is a symptom, physicians should diagnose underlying pathologies that might lead to it instead of focusing only on finding a viable treatment. Physical inactivity negatively impacts on erectile function; experimental and clinical exercise interventions have been shown to improve sexual responses and overall cardiovascular health. Several studies have confirmed that combining the two interventions (mediterranean diet and physical activity) provides additional benefit to erectile function, likely via reduced metabolic disturbances (e.g., inflammatory markers, insulin resistance), decreased visceral adipose tissue, and improvement in vascular function (e.g., increased endothelial function). This brief review shows the main clinical evidences on benefits induced by physical activity on erectile and endothelial dysfunction. The literature shows that erectile dysfunction in middle-aged men is often an early event in endothelial
damage, and physical activity is able to improve both erectile and endothelial dysfunction. Conflicting data regarding the effects of exercise on the androgen status. In clinical practice would be recommended to add regular physical activity to balanced diet and drugs to achieve better therapeutic results.

Introduction

Erectile dysfunction (ED) is experienced at least some of the time by most men who have reached 45 years of age, and it is projected to affect 322 million men worldwide by 2025 and its prevalence is high in men of all ages and increases greatly in the elderly (Seftel et al, 2003). ED's severity and prevalence both increase with aging: since ED is a symptom, physicians should diagnose underlying pathologies that might lead to it instead of focusing only on finding a viable treatment.

Cardiovascular alterations occur in the elderly, and might lead to ED because of penile blood flow impairment: diabetes, smoking, and sedentary life-style, being risk factors for vascular pathologies, can affect erectile function. Metabolic syndrome and psychological factors are highly prevalent in aging men, and might be other important determinants of ED. Drugs play a role in the pathogenesis of ED, as they can alter hormonal or vascular mechanics needed for achieving or maintaining erection. Alterations in penile vessels can be observed in the elderly and in particular lack of androgens might lead to a reduction of smooth muscle cells content in the penis and an increase in the caliber of vascular spaces (Galiano et al, 2010).

About 60% of the elderly population expresses their interest for maintaining sexual activity. Although aging and functional decline may affect sexual function, when sexual dysfunction is diagnosed, physicians should rule out disease or side effects of medications. Common disorders related to sexual dysfunction include cardiovascular disease, diabetes, lower urinary tract symptoms and depression. Early control of cardiovascular risk factors may improve endothelial function and reduce the occurrence of ED. Treating those disorders or modifying lifestyle-related risk factors (eg obesity) may help prevent sexual dysfunction in the elderly (Camacho et al, 2005).

Physical inactivity negatively impacts on erectile function, and experimental and clinical exercise interventions have been shown to improve sexual responses and overall cardiovascular health.
Mediterranean-style diets and a reduction in caloric intake have been found to improve erectile function in men with the aspects of the metabolic syndrome. In addition, several studies have confirmed that combining the two interventions provides additional benefit to erectile function, likely via reduced metabolic disturbances (e.g., inflammatory markers, insulin resistance), decreased visceral adipose tissue, and improvement in vascular function (e.g., increased endothelial function) (Hannan et al, 2009).

There is now a wealth of sophisticated epidemiological evidence to demonstrate that physical activity (PhA) is associated with reduced risk of coronary heart disease, obesity, type 2 diabetes, and other chronic diseases and conditions. Causal relationships between PhA and cardiovascular disease, type 2 diabetes, colon cancer, and all-cause mortality have been recognized for some time. More recently, the pertinent issue has been the dose–response relationship between PhA and health: What is the minimum dose of activity associated with health and well-being? What doses of activity offer greater health benefits? (O’Donovan et al, 2010).

A multidisciplinary approach might be relevant for the treatment of erectile dysfunction, in this context an adequate program of physical activity, especially when there are cardiovascular risk factors, could be very important; to this end, this review summarizes the major findings of the literature about a direct impact of the physical activity on the quality of erection and two of the main factors involved in erectile dysfunction: the endothelial dysfunction and androgen status. Another aim is to stimulate the reader to standardize effective and reproducible protocols of physical activity for clinical practice in this area, to combine with drugs and/or psychological treatment.

**Physical activity and erectile dysfunction**

PhA has proven to be a protective factor for normal erectile function in numerous epidemiological studies.

In a recent study conducted from October 2000 to October 2003 at a university hospital in Italy, fifty-five men randomly assigned to the intervention group received detailed advice about how to achieve a loss of 10% or more in their total body weight by reducing caloric intake and increasing their level of physical activity. Men in the control group (n=55) were given general information about healthy food
choices and exercise. Erectile function score, levels of cholesterol and triglycerides, circulating levels of interleukin 6, interleukin 8, and C-reactive protein, and endothelial function as assessed by vascular responses to l-arginine. After 2 years, body mass index decreased more in the intervention group than in the control group, as did serum concentrations of interleukin 6, and C-reactive protein. The mean level of physical activity increased more in the intervention group than in the control group. The mean of International Index of Erectile Function (IIEF) score improved in the intervention group, but remained stable in the control group. Seventeen men in the intervention group and 3 in the control group reported an IIEF score of 22 or higher. In multivariate analyses, changes in body mass index, physical activity, and C-reactive protein were independently associated with changes in IIEF score (Esposito et al, 2004).

Body mass index (BMI) and physical activity independently and differentially affected ED risk. BMI had greatest influence with low physical activity, and physical activity exerted greatest influence when BMI was high.

In a population representative cross-sectional analytic study of ED in Hong Kong on 1506 subjects (26-70 years), with two-stage stratified random sampling, and face-to-face interviews conducted by trained interviewers with structured questionnaires, was shown that age, physical activity and general psychological distress were independently associated with ED after multivariate adjustments. A relationship between BMI and ED was observed only among men with no exercise (<once/week): using BMI 21.0-21.9 as reference, adjusted for age and smoking status. Being physically active (>or=1000 kcal/week) only reduced the risk of ED in men who were obese, adjusted for age smoking status and BMI (Cheng and Ng, 2007).

In a evaluation of 3,941 adult men (age>or= 20 years) logistic regression analyses were used to examine the relative odds of ED association with categories of BMI, waist circumference (WC), and PhA. PhA level was divided into active (> or =150 min/week), moderately active (30-149 min/week), and inactive (<30 min/week) categories. Moderately active or inactive men had an approximately 40-60% greater odds of ED compared with active men. When all three predictors (WC, BMI, and PhA level) were entered into the same logistic regression model, both a high WC and low PhA level (moderately active
and inactive) were independently associated with a greater odds of ED, whereas BMI level was not. Moderate-intensity PhA (>or =150 min/week) is associated with the maintenance of proper erectile function, regardless of BMI level (Janiszewsky et al, 2009).

In a other study of Esposito et al, a total of 209 subjects were randomly assigned to one of the two treatment groups. The 104 men randomly assigned to the intervention program received detailed advice about how to reduce body weight, improve quality of diet, and increase PhA. The 105 subjects in the control group were given general information about healthy food choices and general guidance on increasing their level of PhA. Erectile function score improved in the intervention group. At baseline, 35 subjects in the intervention group and 38 subjects in the control group had normal erectile function (34% and 36%, respectively). After 2 years, these figures were 58 subjects in the intervention group and 40 subjects in the control group, respectively (56% and 38%). There was a strong correlation between the success score and restoration of erectile function (Esposito et al, 2009).

A recent study on 674 men aged 45-60 yr that included a urological physical examination, medical history, and assessment of testosterone (T) and sex hormone-binding globulin; showed a positive correlation between the IIEF-5 and the Paffenbarger score (PhA index). The IIEF-5 score increased with an increasing Paffenbarger score up to a level of 4000 kcal/wk. T revealed a trend to a significant impact on the IIEF-5 score, but showed no association with the Paffenbarger score. The risk of severe erectile dysfunction (ED) was decreased by 82.9% for males with PhA of at least 3000 kcal/wk compared with males with PhA under 3000 kcal/wk (Kratzik et al, 2009).

Finally, in a recent study a total of 60 patients complaining of erectile dysfunction were evaluated. Patients were assessed at baseline and after 3 months of study treatment; in this study at baseline, patients were randomized to receive phosphodiesterase type 5 inhibitor (PDE5i) alone (group A) or PDE5i plus regular (>=/=3 hours/week), aerobic, non-agonistic PhA (group B). All subjects completed the IIEF-15 questionnaire and were tested for total testosterone (TT). Mean PhA was 3.4 hours/week in group B vs. 0.43 in group A; mean energy expenditure in group B was 1,868 kcal/week or 22.8 metabolic equivalent (MET)/week. IIEF restoration of ED occurred in 77.8% (intervention group) vs. 39.3%
(control). The IIEF-15 score resulted in statistical improvement in intervention group in all the domains but one (orgasm): erectile function 24.7 vs. 26.8; confidence (question 15 on the scale) 3.53 vs. 4.07; sexual desire 6.46 vs. 7.18; intercourse satisfaction 9.85 vs. 11.25; total satisfaction 7.17 vs. 8.07; total score 56.2 vs. 61.07. TT was statistically similar in the two groups; separate analysis in each group showed statistical increase in group B 4.24 vs. 4.55. At multivariate logistic regression analysis, PhA was the only independent variable for normal erection, higher sexual satisfaction and normal total IIEF-15 score (Maio et al, 2010).

**Physical activity and endothelial dysfunction**

Exercise training consistently improves the nitric oxide bioavailability, the number of endothelial progenitor cells (EPC) and also diminishes the level of inflammatory markers, namely pro-inflammatory cytokines and C-reactive protein. However, the mechanisms by which exercise improves endothelial function in coronary artery disease patients are not fully clarified. Several mechanisms have been proposed to explain the positive effect of exercise on the disease progression. They include the decrease in cytokine production by the adipose tissue, skeletal muscles, endothelial cells, and blood mononuclear cells, and also, the increase in the bioavailability of nitric oxide, antioxidant defences, and regenerative capacity of endothelium (Ribeiro et al, 2010).

Regular exercise training augments the number of EPC in patients with cardiovascular risk factors and coronary artery disease and is associated with improved vascular function and nitric oxide (NO) synthesis; in fact, in a recent study, twenty patients with documented coronary artery disease and/or cardiovascular risk factors joined a 12-week supervised running training. Circulating EPC defined by the surface markers CD34, KDR and CD133 were measured at baseline and after exercise training by flow cytometry, with a significant increase in circulating EPCs, which was positively correlated with both, the change of flow mediated dilation (FMD) and the increase of NO synthesis. Plasma vascular endothelial growth factor (VEGF) and erythropoietin did not change in response to exercise. However, there was observed a positive correlation between the number of EPC and erythropoietin at baseline and after training (Steiner et al, 2005).
In another study, EPC were quantified by flow cytometry and cell culture in 25 healthy volunteers undergoing three protocols of running exercise.

Intensive running, defined as 30 min at 100% of the velocity at the individual anaerobic threshold (IAT); approximately 82% maximal oxygen consumption (VO2max), as well as moderate running with 30 min at 80% of the velocity of the IAT (approximately 68% VO2max), increased circulating EPC numbers to 235+/-93% and 263+/-106% of control levels, respectively (Laufs et al, 2005).

A maximal bout of exercise induces a significant shift in CD34+ cells toward CD34+/KDR+ cells, this response was larger in subjects with a less favorable lipid profile.

In another study, healthy subjects (group 1, n = 11; group 2, n = 14) performed a symptom-limited cardiopulmonary exercise test on a bicycle ergometer. Numbers of CD34+/kinase insert domain receptor (KDR)+ cells were determined by flow-cytometric analysis, either after magnetic separation of CD34+ cells (group 1) or starting from whole blood (group 2).

Serum concentrations of VEGF and NO metabolites were measured by using ELISA. Following exercise, EPC increased by 76% (15.4 +/- 10.7 cells/ml vs. 27.2 +/- 13.7 cells/ml) in group 1 and by 69% in group 2 (30.9 +/- 14.6 cells/ml vs. 52.5 +/- 42.6 cells/ml). The increase in EPC correlated positively with LDL and total cholesterol/HDL ratio and negatively with peak oxygen consumption and oxygen consumption at anaerobic threshold. VEGF levels increased with exercise, with a strong trend toward significance. NO levels remained unchanged (Van Craenenbroeck et al, 2008).

The results of another recent study suggest that finishing a marathon race will lead to an inflammatory response and downregulation of circulating hematopoietic stem cells. With respect to EPC no change is observed, which may be because of a greater differentiation of the remaining CD34 cells towards EPC. Sixty-eight healthy marathon runners (age: 57 +/- 6 years) were included in this study. Blood cell counts were evaluated by standard methods, and circulating progenitor cells before and immediately after the race were quantified by fluorescence-activated cell sorter (FACS). VEGF and epidermal growth factor (EGF) was quantified by enzyme-linked immunosorbent assay. A marathon race led to a significant increase in white blood cell count (5283 +/- 155 vs. 13706 +/- 373 cells/ml blood).
Fluorescence-activated cell sorter analysis revealed a significant decrease of CD34 cells (1829+/−115 vs. 1175+/−75 cells/ml blood), CD117 cells (2478+/−245 vs. 2193+/−85 cells/ml blood), and CD133 cells (3505+/−286 vs. 2239+/−163 cells/ml blood). No significant change was observed for EPC defined as CD34/VEGF-R2 cells (117+/−8 vs. 128+/−9 cells/ml blood). With respect to VEGF a significant downregulation was evident directly after the race (48.9+/−8.0 vs. 34.0+/−7.5 pg/ml), whereas no change was obvious in EGF levels (Adams et al, 2008).

Finally, higher habitual PhA level in patients with coronary artery disease was associated with higher FMD and EPC count. Nonetheless, FMD only significantly correlated with increased PhA level, but not EPC, suggesting that increased physical activity improves endothelial function through mechanisms other than increasing EPC count (Luk et al, 2009).

Strenuous activity in healthy individuals leads to a time-dependent increase in EPCs and endothelial microparticles (MPE), that may be related to VEGF and IL-6. In a study, eighteen healthy young men cycled for 4 h continuously at 70% of their individual anaerobic threshold. Peripheral blood was drawn at 16 predefined time points during and after finishing cycling. A significant rise in heart rate and leukocytes was obvious, whereas lactate levels and hematocrit did not change.

The amount of circulating progenitor cells, mature endothelial cells, and microparticles, quantified by flow cytometry, showed a significant time-dependent increase at 210/240 min. In addition a very early rise in VEGF and later increase in IL-6, both measured by ELISA, were evident. All observed changes were normalized 24 h after finishing the test (Mobius-Winkler et al, 2009).

In a recent study on healthy men to 7 days of dry immersion (DI) the authors have investigated endothelial properties before, during, and after 7 days of DI involving eight subjects. Microcirculatory functions were assessed with laser doppler in the skin of the calf and basal blood flow and endothelium-dependent and independent vasodilation were studied.

Also plasma levels of microparticles, a sign of cellular dysfunction, and soluble endothelial factors, reflecting the endothelial state were measured. Basal flow and endothelium-dependent vasodilation were reduced by DI (22 + or - 4 vs. 15 + or - 2 arbitrary units and 29 + or - 6% vs. 12 + or -
6%, respectively), and this was accompanied by an increase in circulating EMP, which was significant on day 3 (42 + or - 8 vs. 65 + or - 10 EMP/microl), whereas microparticles from other cell origins remained unchanged. Plasma soluble VEGF decreased significantly during DI, whereas VEGF receptor 1 and soluble CD62E were unchanged, indicating that the increase in EMP was associated with a change in antiapoptotic tone rather than endothelial activation.

This study showed that extreme physical inactivity in humans induced by 7 days of DI causes microvascular impairment with a disturbance of endothelial functions, associated with a selective increase in EMP. Microcirculatory endothelial dysfunction might contribute to cardiovascular deconditioning as well as to hypodynamia-associated pathologies (Navasiolava et al, 2010).

Our recent study evaluated the effects of a standard protocol of aerobic PhA on quality of erectile dysfunction in patients with arterial ED. Fifty patients (48-62 years) were selected and underwent to standard protocol of aerobic PhA: 150 min of moderate intensity aerobic activity per week (group A). Twenty patients, matched aged, with vascular ED who did not accept to undergo the standard PhA's protocol, represented the control group. All patients were evaluated, by IIEF-5 questionnaire administration, penile echo color doppler and flow-cytometric analysis for detection of serum concentrations of EPC with original immunophenotype [EPC=CD45(neg)/CD34(pos)/CD144(pos)] and EMP [CD45(neg)/CD34(neg)/CD144(pos)].

After 3 months, group A showed IIEF 5 score and peak systolic velocity significantly higher compared to controls, and significantly lower values of acceleration time, in addition serum concentrations of EPC and EMP were significantly lower in group A compared to controls (La Vignera et al, 2011).

Finally, a recent cross-sectional multicenter study with six research groups was undertaken, the purpose of this study was to analyze the relationship of physical activity and dietary pattern to the circadian pattern of blood pressure, central and peripheral blood pressure, pulse wave velocity, carotid intima-media thickness and biological markers of endothelial dysfunction in active and sedentary individuals without arteriosclerotic disease.
Determining that sustained physical activity and the change from sedentary to active as well as a healthy diet improve circadian pattern, arterial elasticity and carotid intima-media thickness may help to propose lifestyle intervention programs. These interventions could improve the cardiovascular risk profile in some parameters not routinely assessed with traditional risk scales. From the results of this study, interventional approaches could be obtained to delay vascular aging that combine physical exercise and diet (Garcia-Ortiz et al, 2010).

**Physical activity and androgen status**

Guilland and colleagues evaluated androgenic status in five well-trained mountaineers during the different phases of a mountaineering expedition during the ascent of Mt Pabil (7,102 m) in the Ganesh Himal massif. In this study androgenic status was evaluated by measuring testosterone glucuronide, Adiol (5 alpha-androstane-3 alpha, 17 beta diol) and 17KS (17-ketosteroids). Reference values were obtained at Chamonix at 1,037 m during rest. During trekking, Adiol and 17-KS decreased. The fall in the urinary androgenic pool persisted during the next phases of the expedition. During the return to sea level, the urinary level of these parameters was still high. (Guilland et al, 1984).

Struder and colleagues investigated hypothalamic-pituitary-gonadal axis regulation in elderly distance runners (RUN; n = 8; age: 68.9 +/- 4.2 yrs; training: 65 +/- 20 km/wk over the last 20 yrs; means +/- SD) and in elderly sedentary individuals (SED; n = 11; age: 69.1 +/- 2.6 yrs) by an aerobic training over 20 weeks (3 times/week, 30-60 min walking), respectively. Results of this study showed that basal plasma free T concentration was significantly lower in RUN (RUN: 10.23 +/- 2.41 pg x ml(-1) vs. SED: 16.6 +/- 5.59 pg x ml(-1)). Lower plasma free T concentrations in RUN compared to SED are not caused by modified LH synthesis-secretion capacity (Struder et al, 1999).

In a cross-sectional study of 400 independently living men between 40 and 80 years of age. Total testosterone, bioavailable testosterone, sex hormone binding globulin (SHBG), estradiol were investigated for their relationship with physical activity. Multivariate analyses showed that higher physical activity score were associated with higher total testosterone and SHBG levels. (Muller et al, 2003).

Another study examined eight endurance-trained males (19-49 years) completed a resting control session and three treadmill runs of 40, 80, and 120 min at 55% of VO2max . Blood samples were drawn before the session and then 1, 2, 3 and 4 h after the start of the run. Plasma was analyzed for luteinizing
hormone (LH) and free and total testosterone. LH was significantly greater at rest compared to the running sessions. Both free and total testosterone generally increased in the first hour of the 80 and 120 min runs and then showed a trend for a steady decline for the next 3 h of recovery. The results indicate that exercise duration has independent effects on the hormonal response to endurance exercise. At a low intensity, longer duration runs are necessary to stimulate increased levels of testosterone and beyond 80 min of running there is a shift to a more catabolic hormonal environment (Tremblay et al, 2005).

In another study hormonal measurements was performed (total testosterone, free testosterone, dehydroepiandrosterone sulfate, estradiol) in a homogenous group of 38 subjects. Among them, was distinguished 22 who had not engaged in any physical activity, and 16 who had recreationally exercised for about 10 years. Both groups did not differ in regard to hormonal status (Medras et al, 2005).

Gray and colleagues evaluated 364 males aged between 20 and 82 comprising a cross-sectional study conducted between 1996 and 1998. Testosterone levels were measured from serum samples obtained between 08:00 and 11:00. In ANCOVA analysis, male testosterone levels differed significantly along this rural-to-urban gradient, with members of the most urban group having higher testosterone levels than groups of farmers and inhabitants of informal housing areas adjacent to towns. Further exploratory ANCOVA analyses revealed that physical activity levels, were not significantly associated with variation in testosterone levels (Gray et al, 2006).

Goh and colleagues, in a study conducted on 531 healthy Singaporean Chinese men aged between 29 and 72 years old using multivariate analyses and adjusting for age and other related factors, showed that exercise, have positive impacts on androgen levels and body composition. (Goh et al, 2007).

In a another recent study the hormonal response to exercise was evaluated in relation to several factors including the intensity, duration, mode of exercise (endurance versus resistance), and training status of the subject. In this study was determined the steroid hormonal response (immediately after a race and 1 week later) to endurance exercise under the real conditions of the classic Athens marathon in a group of well-trained, middle-aged, non-elite athletes. Blood samples were drawn 1 week before the race, directly after completion of the race, and 1 week later. Total testosterone as well as free testosterone dropped significantly 1 h after the race but returned to baseline 1 week later. In this particular group of non-elite, middle-aged marathon runners, the race resulted in an acute decline in testosterone level. The aforementioned changes returned to baseline 1 week later (Karkoulias et al, 2008).
Suzuki and colleagues conducted a cross-sectional analysis of the association of lifestyle factors with circulating concentrations of androstenedione (A-dione), 3-alpha-androstanediol glucuronide (A-diol-g), testosterone (T), SHBG, and free testosterone (FT) among 636 men in the European Prospective Investigation into Cancer and Nutrition. The results of this study showed that physical activity and dietary factors were not associated with androgen concentrations (Suzuki et al, 2009).

Hormonal parameters were measured in a cohort of 387 healthy Caucasian men (aged from 24 to 72 years) from one administrative region of Poland. Their level of physical activity was determined by means of the International Physical Activity Questionnaire (IPAQ). In this study, it was found that contrary to SHBG concentration, total testosterone, free testosterone, bioavailable testosterone, calculated free testosterone and estradiol were negatively associated with age in the investigated subjects. Apart from estradiol, physical activity did not influence concentrations of the studied parameters. In younger (24-48 years), physically active males estradiol was significantly higher than in subjects characterized by a low level of physical activity. The situation was opposite in older males (48-72 years). In this age group, low level of physical activity was associated with lower concentration of estradiol. (Slowinska-Lisowska et al, 2010).

Practical recommendations and special groups with risk factors

Before starting an exercise program should answer the following questions:

a) What dose of physical activity?

b) What frequency of physical activity?

c) What duration of training sessions?

d) What intensity of exercise?

e) What are the risk groups?

What dose of physical activity?

Depending on body weight, 150 min of moderate intensity aerobic activity per week or 75 min of vigorous intensity aerobic activity per week expends around 800–1200 kcal (3349–5023 kJ). Cross sectional studies and exercise interventions suggest that these doses of activity are associated with favourable changes in blood pressure (Cornelissen & Fagard, 2005), lipid and lipoprotein profiles
(Durstine et al., 2001), markers of inflammation (Hamer, 2007), insulin sensitivity (Cornelissen & Fagard, 2005), and other risk factors for chronic diseases (Autenrieth et al., 2009).

**What frequency of physical activity?**

Several studies have shown that taking part in one or two bouts of vigorous-intensity exercise per week can reduce the risk of chronic diseases and premature death (Paffenbarger, 2004).

**What duration of training sessions?**

Although more research is required, there is some evidence that bouts of less than 10 min may also be beneficial to health (Strath et al., 2008).

**What intensity of exercise?**

Physical activity is usually expressed in absolute terms in prospective cohort studies: moderate-intensity is typically characterized as 3–6 METs and vigorous-intensity is typically characterised as 4–6 METs (where one MET is equivalent to the energy expended at rest). There is compelling evidence of a dose–response relationship between physical activity intensity and cardiovascular disease: activities 4–6 METs are associated with lower risk of cardiovascular disease than activities of 3–6 METs, especially in men (Cornelissen & Fagard, 2005; Durstine et al., 2001; Paffenbarger, 2004).

**What are the risk groups?**

There are clinical situations where the management of physical activity can be different, these conditions are differentiated in nonfatal: arthritis, visual impairment, hearing impairment; and fatal conditions: ischemic heart disease, chronic obstructive pulmonary disease, diabetes mellitus, malignant neoplasms (Verbrugge et al., 1995). For these subjects, the recommendation is a gradual achievement of the objectives of physical activity provided for normal adult subjects, but there is no valid references for all categories.
Conclusion

The studies of the literature shows that erectile dysfunction in middle-aged men is often an early event in endothelial damage, and physical activity is able to improve both erectile and endothelial dysfunction. In clinical practice would be recommended to add regular physical activity to balanced diet and drugs to achieve better therapeutic results. Finally, we need to consider possible hormonal changes induced by physical activity and standardize reproducible protocols to be used in clinical practice.

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