ERECTILE DYSFUNCTION

Association Between Penile Color Doppler Ultrasonography and Cardiorespiratory Fitness in Patients With Vascular Erectile Dysfunction

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ABSTRACT

Introduction: Vascular erectile dysfunction (ED) is a burdensome condition, associated with increased cardiovascular risk. Peak systolic velocity (PSV) represents the maximum pulse velocity in the cavernous artery measured by a penile color doppler ultrasonography (PCDU) during a pharmacologically induced erection and is considered a reliable parameter for the diagnosis of vascular ED. However, the cut-off value of standard PSV (30 cm/s) provides high sensitivity only in the diagnosis of advanced arteriogenic disease. Thus, an age-adjusted PSV (6.73 + 0.7 x age cm/s) has been proposed to offer a more accurate diagnosis of vascular ED.

Aim: In this study it was aimed to answer the following question: “Is there any positive association between indexes of vascular erectile dysfunction and cardiorespiratory fitness?”

Main Outcome Measure And Methods: 25 patients with a medical history of ED (median age 55.3 years) underwent PCDU after pharmacological stimulation. Subsequently, a functional evaluation with ECG-monitored, incremental, maximal cardiopulmonary exercise testing was performed.

Results: Peak oxygen uptake (VO2 peak), peak oxygen uptake per body weight (VO2 peak/kg) and Watt/kg correlated with standard PSV, even when corrected for age and BMI (p < 0.05). No differences emerged in cardiopulmonary fitness between pathological and healthy patients (4 vs 21) identified using the standard PSV cut-off. Conversely, the age-adjusted PSV cut-off identified a greater number of patients as pathological (18 vs 7), presenting a significantly lower cardiopulmonary fitness, exercise capacity and efficiency when compared to patients with normal age-adjusted PSV (all p < 0.05).

Conclusion: Data showed an age and BMI independent association between vascular disfunction of cavernous artery and cardiopulmonary fitness, a known solid predictor of all-cause and disease-specific mortality. Moreover, the age-adjusted PSV better identified a subgroup of patients with vascular ED presenting impaired cardiorespiratory fitness and thus increased cardiovascular risk. De Rocco Ponce M, Vecchiato M, Neunhaeuserer D, et al. Association Between Penile Color Doppler Ultrasonography and Cardiorespiratory Fitness in Patients With Vascular Erectile Dysfunction. Sex Med 2021;9:100347.

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Key Words: Erectile dysfunction; Penile color doppler ultrasound; Cardiorespiratory fitness; Cardiovascular risk

INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of morbidity and mortality worldwide. Many biomarkers and associated conditions have been proposed as useful tools to detect early cardiovascular disease. Among others, vascular erectile dysfunction (ED) is particularly interesting as it may suggest an increased risk of CVD even in apparently healthy men.

ED is defined as the persistent inability to achieve or maintain an adequate penile erection for satisfactory sexual intercourse.
This definition describes a symptom (ED) rather than a disease which can be related to different pathological processes (i.e. neurological, endocrinological, tissutal, psychological, relational and vascular impairment), identifying different ED subtypes.

From an epidemiological standpoint, vascular ED is the most frequent, accounting for up to 70% of all cases. Moreover, vascular ED represents an early manifestation of a systemic atherosclerotic process. In fact, it shares many risk factors with other cardiovascular diseases (CVD), that is, obesity, diabetes mellitus, arterial hypertension, hypercholesterolemia and smoking habit. Indeed, previous studies demonstrated that a considerable proportion of patients with vascular ED has angiographically documented silent coronary artery disease. Likewise, other authors observed that among patients older than 45 years with ED of probable vascular pathogenesis, in the absence of any cardiac symptoms, 15.7% showed electrocardiographic alterations during a dynamic ergometric stress test. Montorsi et al. showed that ED can precede coronary and peripheral artery disease of some years and ED onset is associated with subsequent cardiovascular events.

Penile color-doppler ultrasound (PCDU) is the gold standard for vascular ED diagnosis. In fact, PCDU is an important tool to assess penile arterial blood flow and veno-occlusive mechanism. Moreover, PCDU can detect morphological alterations of the walls of cavernous arteries such as increased thickness of intima-media or the presence of atherosclerotic plaques.

Peak systolic velocity (PSV) represents the maximum pulse velocity in the cavernous artery measured by a PCDU during a pharmacologically induced erection and it is considered a reliable parameter for the diagnosis of vascular ED. Kawanishi suggested a possible role of PSV in predicting patients at risk for cardiovascular diseases or peripheral vascular damage. A PSV below 30 cm/s is generally considered diagnostic for penile vascular impairment. In 2006 an age-matched cut-off for PSV, based on the demonstration of concurrent systemic atherosclerosis, was proposed to increase the accuracy in making the diagnosis of vascular ED.

Physical inactivity is considered a relevant risk factor for ED. It is known that physically active individuals have a lower risk of non-communicable chronic diseases, a lower rate of major CV events and a better quality of life. Different studies reported that aerobic exercise and resistance training improve vascular functions.

Physical activity also improves sexual function and cardiovascular health and is associated with a lower risk of ED, with a dose-dependent effect. Although the level of physical activity is a strong prognostic marker for CVD, cardiorespiratory fitness is even a stronger predictor of all-cause and cardiovascular mortality independent of age, sex, ethnicity, and comorbidities.

The best possible evaluation of cardiorespiratory fitness can be indirectly obtained by measuring maximal oxygen consumption (VO2) during incremental cardiopulmonary exercise test, thus analysing the different components of the oxygen transport chain. Peak VO2 is related to the maximal cardiac output and to blood flow and it has been largely used as an indicator of exercise capacity and cardiovascular status. Despite this close association, only few studies investigated the fitness level in patients with vascular ED.

Thus, the purpose of this study was to answer the following question: “Is there any positive association between indexes of vascular erectile dysfunction and cardiorespiratory fitness?”

MATERIALS AND METHODS

Andrological Evaluation

This cross-sectional cohort pilot study involved 25 subjects at their first evaluation for ED at the Andrology and Reproductive Medicine Unit of the University of Padova (Italy) from May 2016 to October 2017. Inclusion criteria were: ED defined as a score of less than 22 in the International Index of Erectile Function (IIEF-5) questionnaire; age between 40 and 70 years. Patients with post-surgical ED, Peyronie’s disease, androgen replacement therapy, history of cardiovascular disease, neoplasia, and end-stage renal or liver disease were excluded. Each patient signed a written consent before enrolling. The research was conducted in accordance with the ethical guidelines of the 1975 Declaration of Helsinki and the procedures have been approved by a local ethics committee. Medical history was collected and blood analyses performed, including fasting plasma glucose, glycated haemoglobin (HbA1c), lipid profile, eGFR, total testosterone and TSH.

All patients underwent a PCDU using a high-resolution color doppler ultrasound (iU22 Philips, Eindhoven, The Netherlands) equipped with a 7–13 MHz probe (axial resolution <0.1 mm). PCDU was performed after an intracavernous injection of alprostadil 10 mcg. A second dose was injected if the obtained erection was inadequate for a proper PCDU procedure. Evaluation of intracavernous blood flow was assessed at the level of the peno-scrotal junction during the following 20 minutes and the PSV was measured when stabilized. All ultrasound examinations were performed by the same operator with experience in vascular diagnostics. None of the patients were prescribed erection inducing medication prior to finalization of the study protocol.

Based on PCDU results, patients were classified in subgroups. We first defined as “normal” a PSV ≥ 30 cm/s and “impaired” a PSV < 30 cm/s using a standard PSV cut-off of 30 cm/s. Then we classified again our patients according to an age-adjusted PSV cut-off, previously defined by our research group and based on the evidence of concurrent systemic atherosclerotic disease. This normal age-adjusted PSV cut-off was calculated as follows: PSV ≥ 6.73 + 0.7 x age. In both cases, patients with a normal PSV, and thus having a non-vascular ED, served as control group. The researchers who performed functional evaluations were not aware of which subgroup each patient was assigned to.

Cardiopulmonary Exercise Testing (CPET)

Each patient was subsequently evaluated at the Sport and Exercise Medicine Division of the University Hospital of Padova.
Cardiorespiratory fitness was assessed by incremental, ECG-monitored, cardiopulmonary exercise testing (Jaeger Master-screen-CPX, Carefusion, Germany, analysed with the JLAB Software). Tests were performed on a bicycle ergometer (eBike, General Electrics). The test protocol consisted in 5-minutes constant load exercise, preceded by 2-minutes of unloaded pedalling. At the end of the constant load exercise, an incremental test of 25 Watts per minute was carried out. During testing, patients were instructed to keep 60-70 rpm and the exercise phase ended at patient exhaustion (Borg rating of perceived exertion (RPE) ≥ 18/20). We considered only maximal tests confirmed by the presence of Respiratory Exchange Ratio (RER) > 1.10, heart rate (HR) ≥ 85% of predicted HR max, and/or plateau of oxygen consumption with increasing workload.34 Oxygen consumption, carbon dioxide output, tidal volume, respiratory frequency and minute ventilation (VE) were analysed breath-by-breath, recorded and averaged every 15 seconds. Exercise test were performed under the supervision of a physician and with defined criteria for stopping as recommended in current guidelines.35 VO2 peak was determined as the highest average VO2 during a 30-s period, while the oxygen uptake efficiency slope (OUES) was calculated as the coefficient of the linear relationship between oxygen uptake and the logarithm of total ventilation.

Statistical Analysis
Statistical analyses were performed with the Statistical Package for Social Science (SPSS Inc., Chicago, IL, USA) ver. 20 software packages. The Shapiro–Wilks test was used to assess the normality of all parameters. Continuous variables are expressed as median and 25th-75th percentile and comparison between subgroup was performed with the Wilcoxon-Mann-Whitney test. Categorical variables were expressed as frequencies and percentages and were compared between groups using Pearson’s chi squared test. The relationship between continuous variables were evaluated by Spearman’s correlation coefficient (r). Independent correlates of PSV were examined by using a multivariate linear regression analysis. All reported probability values are two-tailed and a value of P ≤ 0.05 was considered statistically significant. A statistical power calculation was performed using MedCalc statistical software. For a correlation coefficient of 0.618 (correlation observed between VO2 peak and PSV) and a sample size of n = 25, a statistical power of at least (1 - β) = 90% and α = 5% was obtained.

RESULTS
The baseline characteristics of the 25 included patients are shown in Table 1. All 25 patients completed the study protocol without any complication related to PCDU or CPET procedures. Major comorbidities were dyslipidaemia, arterial hypertension and diabetes mellitus. Eleven patients (44%) were active smokers and seven were former smokers.

Table 1. Characteristics of the study participants.

| Variable                      | Median          | 25th-75th percentile |
|-------------------------------|-----------------|---------------------|
| Age (years)                   | 55.28           | (47.79 - 64.95)     |
| BMI (Kg/m2)                   | 27.75           | (26.57 - 31.14)     |
| SBP (mmHg)                    | 130             | (120 - 140)         |
| DBP (mmHg)                    | 80              | (70 - 90)           |
| Total testosterone (nmol/L)   | 13.64           | (9.46 - 17.21)      |
| HbA1c (mmol/mol)              | 38.5            | (35.25 - 46.75)     |
| Glycaemia (mg/dl)             | 104             | (95.00 - 122.0)     |
| Total cholesterol (mg/dl)     | 209             | (177 - 230)         |
| HDL cholesterol (mg/dl)       | 50              | (35 - 63)           |
| LDL cholesterol (mg/dl)       | 127             | (111 - 156)         |
| Triglycerides (mg/dl)         | 106             | (64 - 171)          |

| VARIABLE | No | % |
|----------|----|---|
| Smokers  | 11 | 44|
| Hypertension | 12 | 48|
| Dyslipidaemia | 15 | 60|
| Diabetes mellitus | 6  | 24|

BMI = body mass index; SBP/DBP = systolic/diastolic blood pressure; HbA1c = glycated hemoglobin.

<sup>P</sup> = .002, maximal work rate (<sup>P</sup> = .476, <sup>P</sup> = .016) and maximal work rate/kg (<sup>P</sup> = .591, <sup>P</sup> = .002). This correlation with VO2 peak/kg (<sup>R</sup><sup>2</sup> = 0.382, <sup>P</sup> = .014) and maximal work rate/kg (<sup>R</sup><sup>2</sup> = 0.384, <sup>P</sup> = .020) remained statistically significant after correcting for age and BMI as represented in Figure 1.

Furthermore, we divided our population according to PSV criteria in normal and impaired penile vascular function: a “standard” PSV cut-off of 30 cm/s and an age-matched PSV cut-off as previously described.16 Four patients showed an impaired PSV value using the standard cut-off used to identify vascular impairment, while the age-adjusted PSV cut-off identified 18 patients as pathological. When comparing the subgroups of patients having normal PSV and those with impaired PSV according to each PSV threshold, no statistically significant difference was found regarding BMI, total testosterone, smoking habit, hypertension, diabetes mellitus and dyslipidaemia (Table 2).

However, cardiorespiratory fitness was significantly reduced in patients with impaired age-adjusted PSV, showing lower absolute VO2 peak, VO2 peak per body weight, maximal work rate, time to exhaustion and peak heart rate (all <sup>P</sup> < .05). This was also confirmed by a statistical trend of the OUES. Although all participants presented on average normal values of VE/VCO2 slope, ventilation was found to be more efficient in patients with normal age-adjusted PSV (lower VE/VCO2 slope, <sup>P</sup> = .009). No differences emerged in cardiopulmonary fitness between patients with normal vs pathological PSV identified using the standard PSV cut-off (Table 2).

DISCUSSION
The aim of this study was to investigate the relationship between cardiorespiratory function and indexes of vascular...
erectile function in patients with ED. Indeed, only few studies evaluated cardiopulmonary fitness in this population31–33 and to the best of our knowledge, no studies have yet investigated a possible association between doppler alterations of cavernous arteries and aerobic exercise capacity.

The main findings of this study are: (i) Vascular ED correlates with aerobic capacity, independently of age and BMI; (ii) an age-adjusted PSV cut-off is more accurate in identifying patients with impaired cardiorespiratory fitness and thus higher cardiovascular risk.

Association between PSV and cardiorespiratory fitness: Our results showed a significant association between the main parameter evaluating penile vascular dysfunction, that is, PSV, and cardiopulmonary fitness and/or maximal aerobic power. Moreover, multivariate linear regression analyses showed a significant correlation between PSV and VO2 peak/kg, also after considering age and BMI as confounders. Our results are consistent with previously published papers in this field. In a recent study of Kumagai et al, VO2 peak and muscle strength resulted significantly associated with the IIEF-5 score after considering confounders, including age and testosterone serum level.36 Compostella et al in 2017 evaluated physical performance in a group of patients with history of ED, admitted to intensive cardiac rehabilitation after an acute myocardial infarction. They reported a significantly lower VO2 peak and a negative correlation with severity of ED.37 Thus, a link between aerobic capacity and male sexual function might be possible, and it may be related to vascular and endothelial function. Indeed, vascular ED is a marker of vascular disease, affecting the cavernous arteries and the coronary and peripheral vessels as well.38,39 Thus, the presence and degree of vascular ED, expressed by a reduced PSV value, could be a sign of systemic vascular disease, which provokes a reduced exercise tolerance. It should be mentioned that it is possible to find a normal PSV in ED due to a high diastolic velocity. This situation is frequently related to anxiety during the exam when catecholamines cause an insufficient relaxation of cavernous smooth muscle thus preventing a proper vein occlusion. In this case, however, the penile hemodynamic should be considered normal. On the other hand, an impaired PSV is certainly a pathological condition and directly related to vascular ED. In other words, PSV can be considered a highly specific parameter to diagnose vascular ED.

Standard PSV versus age-adjusted PSV: In our study, only 4 patients presented an impaired PSV, using a standard cut-off value of 30 cm/s while the age-adjusted PSV threshold identified 18 patients as pathological. This difference prompts the question about which PSV threshold better identifies patients with an early cardiovascular impairment and therefore higher cardiovascular risk.

As expected, each PSV cut-off value identified a group with an impaired penile vascular function in which common risk factors for CVD tended to be higher or more prevalent compared to patients with a normal PSV, although these differences between subjects with normal vs impaired PSV did not reach a statistical significance.

Regarding the cardiopulmonary fitness and efficiency, a standard 30 cm/s PSV cut-off did not discriminate between subject with different aerobic and functional exercise performance. Conversely, those subjects identified as “pathological” according to the age-related PSV cut-off presented a significantly lower cardiopulmonary fitness, maximal exercise capacity and ventilatory efficiency. Thus, although both subgroups with impaired penile vascular function, as determined with the different cut-offs, showed generally lower levels of aerobic and exercise capacity, only the age-related PSV cut-off value was able to identify patients with a significantly reduced cardiopulmonary fitness and efficiency. This might indicate that the age-adjusted method is more sensitive in early detecting patients with higher CV risk. Actually, the PSV cut-off value of 30 cm/s used to diagnose penile arterial impairment is based on old studies that compared PSV with selective arteriography, thus detecting only overt stenosis of cavernous arteries.15 For this reason, the cut-off value of

Figure 1. Relationship between peak systolic velocity (PSV) and peak oxygen uptake per kilogram of body weight (VO2 peak/kg), corrected for age and BMI, obtained at cardiopulmonary exercise test.

$R^2 = 0.382$

$P = 0.014$
standard PSV provides high sensitivity only in the diagnosis of advanced vascular disease. Indeed, a reduced cardiopulmonary fitness is a strong and independent predictor of CVD and all-cause mortality. Since it is known that cardiopulmonary fitness will decrease with age and due to the fact that age-related PSV cut-off was specifically adjusted for age, it is not

Table 2. Clinical features and CPET parameters for patients with and without vascular erectile dysfunction.

|                | Standard PSV | Age-matched PSV |
|----------------|--------------|-----------------|
|                | Normal PSV21 patients | Impaired PSV4 patients | P | Normal PSV7 patients | Impaired PSV8 patients | P |
| Age (years)    | 55.09        | 60.27           | .592 | 46.90 | 59.20 | .005 |
| (47.79 - 62.93) | (48.10 - 67.62) |                |     | (43.2 - 55.1) | (50.3 - 66.7) |     |
| BMI (Kg/m²)    | 27.18        | 30.71           | .496 | 27.18 | 29.75 | .178 |
| (26.57 - 31.14) | (27.34 - 31.60) |                |     | (24.59 - 28.40) | (26.59 - 31.88) |     |
| Total testosterone (nmol/L) | 14.08 | 9.59 | .625 | 13.89 | 13.64 | .953 |
| (9.42 - 17.30) | (8.53 - 10.30) |                |     | (7.47 - 17.09) | (10.14 - 16.36) |     |
| CVD risk factors |              |                  |     |       |       |     |
| Hypertension   | 9 (43%)      | 3 (75%)         | .238 | 3 (43%) | 9 (50%) | .784 |
| Diabetes       | 4 (19%)      | 2 (50%)         | .184 | 0 (33%) | 6 (33%) | .080 |
| Dyslipidaemia  | 13 (62%)     | 2 (50%)         | .656 | 3 (67%) | 12 (67%) | .275 |
| Smoking habit  | 9 (43%)      | 2 (50%)         | .792 | 3 (44%) | 8 (44%) | .943 |
| CPET Peak parameters |             |                  |     |       |       |     |
| HR peak (bpm)  | 164 (146 - 175) | 152 (149 - 167) | .452 | 171 (166 - 193) | 154 (147 - 172) | .041 |
| HR peak (% predicted) | 98.48 | 97.87 | .803 | 99.36 | 97.19 | .270 |
| (90.44 - 108.21) | (92.71 - 99.65) |                |     | (90.66 - 104.89) |                |     |
| HRRmax (bpm)   | 94 (76 - 105) | 83 (630 - 101) | .452 | 99 (94 - 119) | 88 (73 - 103) | .074 |
| VO2 peak (ml/min) | 2537 | 2049 | .203 | 3130 | 2396 | .021 |
| VO2 peak/kg (ml/kg/min) | 29.52 | 23.78 | .331 | 36.40 | 27.10 | .003 |
| VO2 peak (% predicted) | 112 (84 - 124) | 100 (87 - 109) | .409 | 119 (100 - 125) | 101 (82 - 119) | .357 |
| RER peak       | 1.9 (1.14 - 1.29) | 1.19 (1.15 - 1.19) | .803 | 1.16 (1.10 - 1.28) | 1.20 (1.16 - 1.27) | .270 |
| Max power output (W) | 200 (158 - 225) | 150 (128 - 206) | .177 | 225 (195 - 255) | 178 (155 - 225) | .029 |
| Max power output/kg (W/kg) | 2.32 (1.72 - 2.55) | 1.71 (1.53 - 2.22) | .203 | 2.62 (2.32 - 3.33) | 2.13 (1.49 - 2.47) | .009 |
| Other CPET parameters |             |                  |     |       |       |     |
| OUES (mL/logL) | 2604 (2094 - 2923) | 2078 (1860 - 2821) | .452 | 2793 (2604 - 3174) | 2313 (1913 - 2845) | .055 |
| Time to exhaustion (s) | 869 (744 - 1011) | 826 (761 - 878) | .592 | 986 (877 - 1149) | 811 (730 - 900) | .012 |
| VE/VCO2 slope | 25.10 (23.59 - 27.65) | 27.30 (25.86 - 29.32) | .081 | 24.02 (22.83 - 25.10) | 26.85 (24.93 - 28.52) | .009 |
surprising that patients’ age might appear a confounding factor. However, it is known that lower cardiorespiratory fitness is associated with higher CV risk independently of age.29 and it is also known that the incidence of vascular ED will increase with age.42 Thus, it seems logical to detect a higher rate of vascular ED using the age-matched PSV cut-off in patients who also showed lower levels of cardiopulmonary fitness. Moreover, the PSV was shown to directly correlate with VO₂ peak/kg, independently of age. This might reinforce the validity of parameters of cardiopulmonary fitness as prognostic markers also for vascular ED and the clinical significance of the age-related PSV as a diagnostic tool.

Additional interesting data show a reduced exercise tolerance associated with a decreased ability to increase heart rate during incremental exercise testing in patients with impaired age-adjusted PSV. This chronotropic incompetence might be due to a lower exercise tolerance or could be considered as an early sign of cardiac autonomic dysfunction. This is not surprising if we consider that a normal erectile function requires an autonomic nervous system that works adequately as well. In this regard, different studies suggested that cardiac autonomic function could be impaired in several patients with ED.43−45

Erectile dysfunction, vascular health and cardiorespiratory fitness: Overall these data point out the profound connection between ED, vascular health and cardiorespiratory fitness. Actually, both American and European guidelines on erectile dysfunction include lifestyle modification and physical activity as part of ED treatment.36,47 For their established beneficial effect on vascular ED management, more consideration should be given to lifestyle modifications, as first-line therapy. Indeed, pharmacotherapy remains the most used treatment for vascular ED and it has proven to be an excellent short-term approach, but lifestyle modification are crucial for a long-term improvement. Exercise capacity may be potentially improved by an increase in physical activity levels. Furthermore, physical activity and exercise are an effective, non-invasive, and non-pharmacologic intervention for ED.48 Many different reviews demonstrated that physical activity has a protective effect from vascular ED26,27,49−51 and tried to define a correct level of exercise and lifestyle interventions recommended to treat this disease.27,52−54 As men age, they tend to become more physically inactive thus increasing their risk of ED. Therefore, regular physical activity and exercise represent a great resource to prevent and treat ED and should be considered the first-line treatment option for most of these patients.

Clinical significance: This study confirms and emphasises the clinical significance of a sexual symptom such as ED as a marker of global health. Due to the tight association between vascular ED and cardiorespiratory fitness, men with ED should always be assessed and screened for the presence of underlying vascular pathological conditions and cardiovascular risk factors in order to prevent the progression of atherosclerosis and to decrease the incidence of subsequent major cardiovascular events. Indeed, maximal exercise testing should be regularly performed in all patients with chronic diseases, particularly when affecting the cardiovascular system.55,56 Moreover, a tailored exercise training prescription may lead to improved cardiorespiratory fitness having a positive impact on CV risk and ED.57

Limitations and perspectives: The main limitation of this study is the low sample size, which could explain why common CV risk factors were not found statistically more prevalent in patients with an impaired PSV. Nevertheless, the association between PSV and cardiopulmonary fitness is in line with previously published data showing a correlation between the severity of erectile dysfunction and physical performance. Future prospective and controlled longitudinal studies with larger sample size should investigate, in more homogeneous study populations, the specific effects of aerobic and strength exercise on cardiopulmonary fitness and PSV, to establish a possible direct relationship as well.

CONCLUSION

In conclusion, this is the first study showing an age and BMI independent association between vascular dysfunction of cavernous artery, expressed by PSV, and cardiopulmonary fitness, a known marker and strong predictor of all-cause and disease-specific mortality. Moreover, in patient with an history of ED, performing a PCDU and using an age-adjusted PSV cut-off may help to better identify those patients presenting with impaired cardiorespiratory fitness and thus increased CV risk. This study may help to reinforce the role of exercise capacity and, in wider terms, of physical activity, in preventing and possibly treating ED.

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