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Role of High Physical Fitness in Deterioration of Male Sexual Function in Japanese Adult Men

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Abstract

Male sexual function is regulated by vascular function and impaired vascular function is closely related with erectile dysfunction (ED). Vascular functions are positively influenced by physical fitness (i.e., aerobic capacity, muscle strength, and flexibility). The detailed associations between physical fitness and male sexual function remain poorly understood. The present study aimed to clarify the influence of physical fitness on male sexual function. In 177 adult men, peak oxygen consumption ($VO_{2\ peak}$), handgrip strength (HGS), and sit and reach were measured as indices of physical fitness. Arterial stiffness and erectile function were assessed by carotid–femoral pulse wave velocity (cfPWV) and the International Index of Erectile Function 5 (IIEF5) questionnaire, respectively. IIEF5 score was significantly correlated with $VO_{2\ peak}$ ($r_s = 0.52$), HGS ($r_s = 0.37$), and cfPWV ($r_s = -0.44$); and multivariate linear regression analyses showed that $VO_{2\ peak}$, HGS, and cfPWV were significantly associated with IIEF5 score after considering confounders. The receiver operator characteristic curve analysis suggested that the cutoff values for predicting ED were 29.0 ml/min/kg for $VO_{2\ peak}$ and 39.3 kg for HGS. The IIEF5 score was the highest in the subjects with the values of both $VO_{2\ peak}$ and HGS were higher than their respective cutoff values, while the IIEF5 score was the lowest in the subjects with the values of both $VO_{2\ peak}$ and HGS were lower than their respective cutoff values. These results suggest that the maintenance of high aerobic capacity and muscular strength may offset deterioration of male sexual function.

Keywords

erectile dysfunction, exercise capacity, aerobic fitness, muscular strength, arterial stiffness

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Erectile dysfunction (ED), defined as the inability to attain or maintain penile erection that is sufficient for satisfactory sexual performance (Yafi et al., 2016), is a common clinical problem worldwide. The Massachusetts Male Aging Study identified that the prevalence of mild-to-moderate ED is 52% in men aged 40–70 years (Feldman, Goldstein, Hatzichristou, Krane, & McKinlay, 1994), which suggests that ED is widely prevalent among middle-aged and elderly men. ED has been previously reported to be associated with depressive symptoms (Nelson, Mulhall, & Roth, 2011) and has been observed to affect the quality of life (QOL) negatively (Yafi et al., 2016). In addition, a previous meta-analysis has revealed that men with ED exhibited 48% higher risk of cardiovascular disease (CVD) than men

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without ED (Dong, Zhang, & Qin, 2011). The assessment of male sexual function and prevention of age-related deterioration of male sexual function are necessary for better QOL and for preventing occurrence of CVD in future.

Erectile function is regulated by vascular function and impaired vascular function is closely related with deterioration of male sexual function (Kumagai, Yoshikawa, Myoenzono, et al., 2018; Montorsi, Montorsi, & Schulman, 2003; Montorsi et al., 2005; Vlachopoulos, Aznaouridis, et al., 2008; Vlachopoulos, Ioakeimidis, Terentes-Printzios, & Stefanadis, 2008). Previously, it has been reported that physical fitness, such as aerobic capacity (Myers et al., 2002), muscular strength (Leong et al., 2015), and flexibility (Komatsu et al., 2017; Yamamoto et al., 2009), are associated with CVD and its risk factors, including vascular function. In addition, a lot of studies have demonstrated that interventions of aerobic exercise (Maeda et al., 2009; Matsubara et al., 2014; Tanahashi et al., 2014; Tanaka et al., 2000; Tomoto, Sugawara, Nogami, Aonuma, & Maeda, 2015), low-intensity resistance exercise (Okamoto, Masuhara, & Ikuta, 2011), and stretching exercise (Cortez-Cooper et al., 2008; Nishiwaki, Yonemura, Kurobe, & Matsumoto, 2015) improve vascular functions. On the other hand, a recent meta-analysis has demonstrated that physical activity and regular exercise are effective for improving sexual functions in self-reporting ED patients (Silva, Sousa, Azevedo, & Martins, 2017). Taken together, these previous studies have implied that physical fitness is associated with sexual function through vascular function in men. However, detailed associations between physical fitness, male sexual function, and vascular function remain poorly understood.

The present study hypothesized that men with high physical fitness exhibit high male sexual function due to low arterial stiffness and aimed to clarify the role of high physical fitness, such as aerobic capacity, muscular strength, and flexibility, for preventing ED. To test this hypothesis, male sexual function, physical fitness, and arterial stiffness were cross-sectionally assessed in adult men.

Methods

Participants

The subjects of the present study were recruited using local newspaper advertisements. A total of 177 adult men participated in this study (age: 23–82 years, body mass index [BMI]: 17.3–33.6 kg/m^2). Antihypertensive, antidyslipidemic, hypoglycemic, and sleep-inducing medications were used by 12 (6.8%), 13 (7.3%), 3 (1.7%), and 2 participants (1.1%), respectively. Participants who ate, took medicines in the morning of the measurement day, and who were undergoing treatment for ED were excluded from the present study. No participants had a history of angina, myocardial infarction, stroke, depression, and prostatic hypertrophy, and no participants were current smokers. This study was approved by the ethical committees of the Institute of Health and Sport Sciences of University of Tsukuba. The study conformed to the principles outlined in the Helsinki Declaration, and all participants provided written informed consent before inclusion in the study.

Anthropometric Measurements

Body weight was measured to the nearest 0.1 kg using a digital scale. Height was measured to the nearest 0.1 cm using a wall-mounted stadiometer. BMI was calculated as the participants' weight (kg) divided by their height squared (m^2). Waist circumference was directly measured at the level of the umbilicus, with the participant in a standing position; measurements were duplicated to the nearest 0.1 cm.

Blood Biochemistry

Blood samples were obtained in the morning after a 12-hr overnight fast. Serum concentrations of triglyceride, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and plasma concentration of glucose and hemoglobin A1c (HbA1c) were determined using standard enzymatic techniques. Serum total testosterone levels were measured using chemiluminescent immunoassay by a commercial laboratory (LSI Medience, Ibaraki, Japan).

Physical Fitness

With regard to physical fitness, the subjects performed peak oxygen consumption ($VO_{2\ peak}$) for aerobic capacity, handgrip strength (HGS) for muscular strength, and sit and reach for flexibility. To evaluate aerobic capacity, the subjects performed an incremental cycling ergometer exercise consisting of 2 min at 20 W, followed by a 10–20 W increase every 1 min (<50 years, 20 W/min; >50 years, 10 W/min). Aerobic fitness was measured using an online computer-assisted circuit spirometry (AE300S; Minato Medical Science, Osaka, Japan) and $VO_{2\ peak}$ was assumed when at least two of the following criteria were satisfied: (a) the participant reaching the age-predicted maximal heart rate (i.e., 220 − age), (b) Borg scale >19, (c) respiratory equivalent >1.2, or (d) the participant being unable to maintain a pedaling speed <55 rpm (Sugawara et al., 2012). As an index of muscular strength, HGS was measured by use of a Takei dynamometer (T.K.K.5401; Takei Kiki Kogyo, Niigata, Japan). This was assessed with reference to the guideline of the Japanese Ministry of Education, Culture, Sports, Science, and Technology. Flexibility was measured by a sit-and-reach test using a flexibility-testing device. Subjects were seated on the floor, with the hip, back, and occipital region of the head touching the wall, legs held straight by the tester, and both hands put on the device with their arms held straight, and the device was set to zero. Participants were then asked to slowly bend forward and reach as far forward as possible. The best out of two trials was recorded.

Heart Rate, Blood Pressure, and Arterial Stiffness

After a resting period of at least 20 min, heart rate, blood pressure, and arterial stiffness were measured in a quiet, temperature-controlled room (24–26°C). Heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure, and carotid–femoral pulse wave velocity (cfPWV) were measured using a previously described noninvasive vascular profiling system (form PWV/ABI; Colin Medical Technology, Komaki, Japan; Kumagai, Yoshikawa, Myoenzono, et al., 2018). Eighty percent of the direct carotid–femoral distance was applied to calculate cfPWV (Van Bortel et al., 2012). Carotid and femoral artery pulse waves were simultaneously obtained using two applanation tonometers incorporating an array of 15 micro-piezoresistive transducers. Bilateral brachial and posterior tibial arterial pressure waveforms were recorded using extremity cuffs connected to air plethysmographic sensors wrapped on both arms and ankles of the participants. The distances traveled by the pulse waves were assessed in triplicate with a random zero-length measurement over the surface of the body using a nonelastic tape measure. Pulse wave transit time was determined from the time delay between the proximal and distal "foot" waveforms. The foot of the wave was automatically identified and detected as the commencement of a sharp systolic upstroke. PWV was assessed in duplicate and was calculated as the distance divided by the transit time.

Erectile Function

The International Index of Erectile Function (IIEF) questionnaire, developed and validated in 1997 (Rosen et al., 1997) has been adopted as the gold standard assessment for ED (Rosen, Cappelleri, Smith, Lipsky, & Pena, 1999). The IIEF5, the shortened form of the IIEF, was used for assessment of erectile function. The IIEF5 score ranges from 5 to 25 points and a descending score indicates worsening of erectile function. Based on previous studies, individuals with a score of 5–7 points on the IIEF5 were diagnosed with severe ED, whereas a score of 8–11 points, 12–16 points, 17–21 points, and 22–25 points indicated moderate, mild-to-moderate, mild, and no ED, respectively (Bohm et al., 2010; Rosen et al., 1999).

Statistical Analysis

The Shapiro–Wilk test was used to assess the normality of all parameters. Data are expressed as the mean ± *SD* or frequency counts (for categorical data). Values were analyzed by using Spearman rank correlation coefficients (r_s). The variables of skewed distributions have been log-transformed, after obtaining a normal distribution, before multivariate linear regression analysis. Independent correlates of log-transformed IIEF5 were examined by using a multivariate linear regression analysis. To define the area under the curve (AUC) and for the calculation of optimal cutoff values for predicting ED, the receiver operator characteristic (ROC) curve analysis was used. The participants were stratified based on whether the values of the HGS and $VO_{2\ peak}$ were above or below the cutoff values of HGS and $VO_{2\ peak}$ calculated by ROC analysis. Statistical significance was set a priori at $p <$ .05 for all comparisons. Statistical analyses were performed using JMP Pro version 12 (SAS Institute).

Results

The characteristics of the subjects are summarized in Table 1. The mean values of BMI (22.6 kg/m^2), waist circumference (81.2 cm), total cholesterol (213 mg/dl), HDL cholesterol (65 mg/dl), LDL cholesterol (124 mg/dl), triglycerides (100 mg/dl), glucose (102 mg/dl), HbA1c (5.5 mg/dl), testosterone (21.6 nmol/L), SBP (124 mmHg), and DBP (78 mmHg) were within the normal range.

$VO_{2\ peak}$ was significantly correlated with age ($r_s = -0.62$, $p < .001$), height ($r_s = 0.30$, $p < .001$), waist circumference ($r_s = -0.62$, $p < .001$), HDL cholesterol levels ($r_s = 0.22$, $p = .004$), triglyceride levels ($r_s = -0.21$, $p = .005$), glucose levels ($r_s = -0.33$, $p < .001$), HbA1c levels ($r_s = -0.40$, $p < .001$), serum testosterone levels ($r_s = 0.26$, $p = .001$; Figure 1), cfPWV ($r_s = -0.44$, $p < .001$; Figure 1), and IIEF5 score ($r_s = 0.52$, $p < .001$; Figure 1). In addition, HGS was significantly correlated with age ($r_s = -0.49$, $p < .001$), height ($r_s = 0.54$, $p < .001$), HbA1c ($r_s = -0.24$, $p = .001$), cfPWV ($r_s = -0.25$, $p < .001$; Figure 1), and IIEF5 score ($r_s = 0.37$, $p < .001$; Figure 1), but not serum testosterone levels ($r_s = 0.06$, $p = .394$; Figure 1). There were no significant associations between sit-and-reach score and serum testosterone levels ($r_s = 0.06$, $p = .421$), cfPWV ($r_s = -0.06$, $p = .394$), and IIEF5 score ($r_s = 0.08$, $p = .265$; Figure 1). On the other hand, IIEF5

Table 1. Characteristics of Studied Men ($n = 177$).

Variable	$n = 177$
Age, years	57±16
Height, cm	167.8±6.6
Body mass, kg	63.7±8.8
Body mass index, kg/m^2	22.6±2.6
Waist circumference, cm	81.2±8.5
Total cholesterol, mg/dl	213±35
HDL cholesterol, mg/dl	65±15
LDL cholesterol, mg/dl	124±33
Triglycerides, mg/dl	100±47
Glucose, mg/dl	102±20
HbA1c, mg/dl	5.5±0.5
Testosterone, nmol/l	21.6±6.5
$VO_{2\ peak}$, ml/min/kg	28.6±8.3
Grip strength, kg	38.9±6.1
Sit and reach, cm	35.0±9.0
Heart rate, bpm	60±9
Systolic blood pressure, mmHg	124±14
Diastolic blood pressure, mmHg	78±10
cfPWV, cm/s	876±181
IIEF5 score, points	18±5

Note. Data are shown as the mean ± *SD* or frequency counts (%), as appropriate. cfPWV = carotid–femoral pulse wave velocity; HbA1c = hemoglobin A1c; HDL = high-density lipoprotein; IIEF5 = International Index of Erectile Function 5; LDL = low-density lipoprotein; $VO_{2\ peak}$ = peak oxygen consumption.

scores were significantly correlated with age ($r_s = -0.56$, $p < .01$), height ($r_s = 0.35$, $p < .01$), glucose levels ($r_s = -0.26$, $p < .01$), HbA1c levels ($r_s = -0.43$, $p < .01$), testosterone levels ($r_s = 0.18$, $p < .05$), and cfPWV ($r_s = -0.44$, $p < .01$).

Table 2 presents the independent correlates of log-transformed IIEF5 score. The log-transformed IIEF5 scores were significantly associated with cfPWV ($\beta = -0.179$, $p = .028$), $VO_{2\ peak}$ ($\beta = 0.243$, $p = .004$), and HGS ($\beta = 0.169$, $p = .037$) after considering age and serum testosterone levels.

To define the calculated cutoff values of $VO_{2\ peak}$ and HGS for predicting ED, ROC analysis was applied separately. According to ROC analysis, the best applicable cutoff values for predicting ED were 29.0 ml/min/kg for $VO_{2\ peak}$ (AUC = 0.752; Figure 2A) and 39.3 kg for HGS (AUC = 0.688; Figure 2B). Figure 3 presents the combined effects of $VO_{2\ peak}$ and HGS on IIEF5 score and cfPWV. The participants were stratified based on whether the values of HGS and $VO_{2\ peak}$ were higher or lower than the cutoff values of the HGS and $VO_{2\ peak}$ calculated by ROC analysis. The IIEF5 score was the highest in the subjects with the values of both HGS and $VO_{2\ peak}$ higher than their respective cutoff values (21.8 ± 3.6 points), while the IIEF5 score was the lowest in the subjects with the values of both HGS and $VO_{2\ peak}$ lower than their respective cutoff values (15.4 ± 5.3 points). The subjects with only one of the HGS or $VO_{2\ peak}$ values higher than their respective cutoff values showed significantly lower or higher IIEF scores (18.2 ± 4.3 points) than the subjects with both HGS and $VO_{2\ peak}$ values higher and lower than their cutoffs, respectively. Similarly, cfPWV was the lowest in the subjects with both the HGS and $VO_{2\ peak}$ values higher than their respective cutoff values (767 ± 120 cm/s), while the cfPWV was the highest in the subjects with both the HGS and $VO_{2\ peak}$ values lower than their respective cutoff values (959 ± 196 cm/s). Subjects with either one of the values of the HGS or $VO_{2\ peak}$ higher than its cutoff value showed significantly higher or lower cfPWV (859 ± 155 cm/s) than that in the subjects with both the HGS and $VO_{2\ peak}$ values higher and lower, respectively.

Discussion

The present study investigated the associations between physical fitness, male sexual function, and vascular function. $VO_{2\ peak}$ and HGS were significantly correlated with both male sexual function and arterial stiffness; and the multivariate linear regression analyses showed that the $VO_{2\ peak}$, HGS, and cfPWV were significantly associated with male sexual function after considering confounders, including age and testosterone. In addition, ROC analyses suggested that the cutoff values for predicting ED were 29.0 ml/min/kg for $VO_{2\ peak}$ and 39.3 kg for HGS. The IIEF5 score was the highest in the subjects with the values of both $VO_{2\ peak}$ and HGS higher than their respective cutoff values, while the IIEF5 score was the lowest in the subjects with the values of both $VO_{2\ peak}$ and HGS lower than their respective cutoff values. These findings suggest that high physical fitness may offset the aging-induced deterioration of male sexual function through low arterial stiffness.

Several studies (Cheng & Ng, 2007; Kalter-Leibovici et al., 2005; Minami et al., 2017) and recent meta-analysis (Silva et al., 2017) have demonstrated that physical activity is effective for improving sexual functions in patients with type 2 diabetes mellitus, obesity, and ED. Similarly, it has been reported that sedentary lifestyle and sitting time increase the risk of ED (Bacon et al., 2003; Furukawa et al., 2017; Selvin, Burnett, & Platz, 2007). Previous evidences have suggested that exercise programs are associated with improving ED in patients with cardiac diseases (Begot et al., 2015; Meldrum et al., 2011). These previous studies implied that physical fitness is associated with male sexual function. The detailed association between physical fitness and male sexual function has remained poorly understood. The present study found that aerobic capacity and

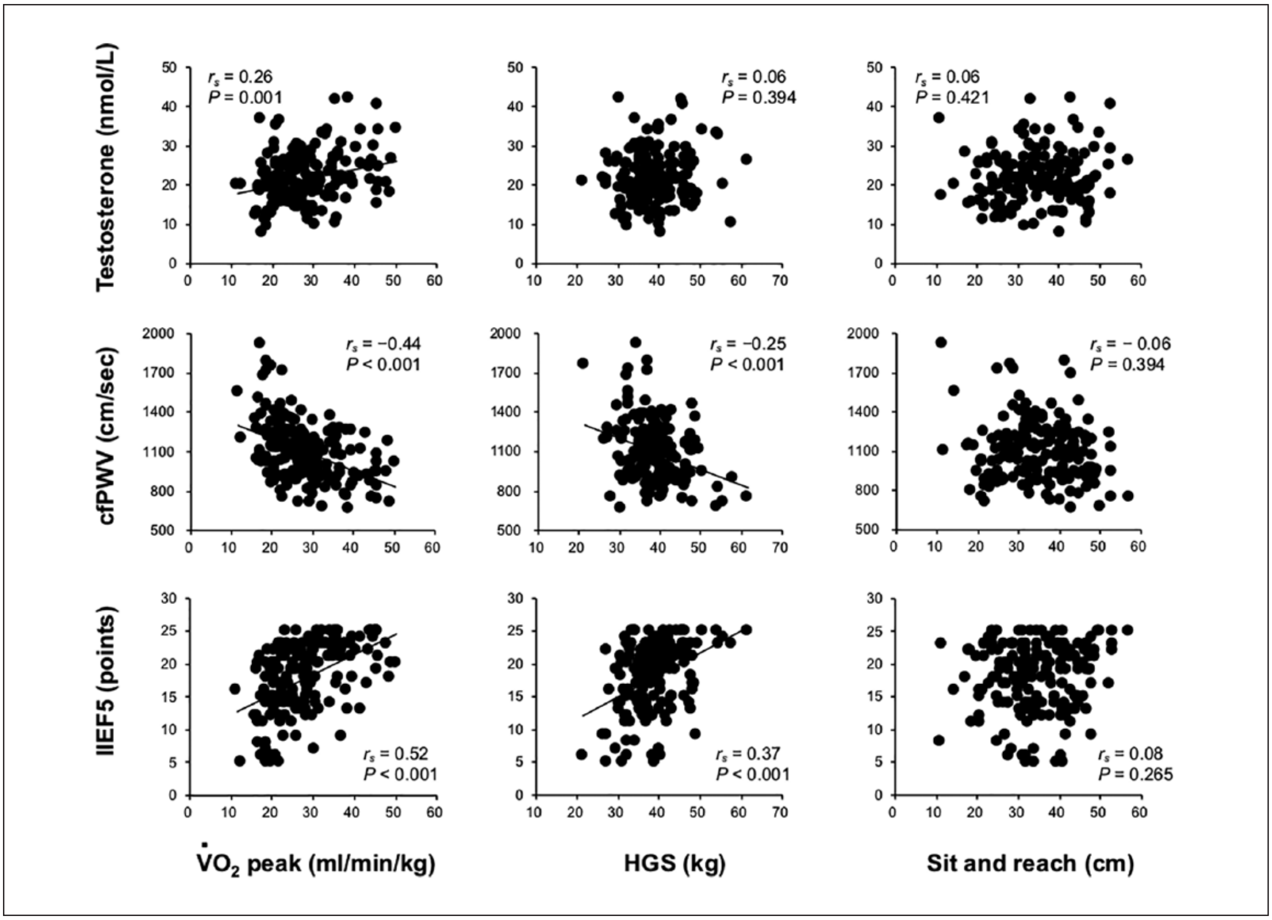

Figure 1. Correlations between physical fitness and serum testosterone levels, cfPWV, and IIEF5 scores.
cfPWV = carotid–femoral pulse wave velocity; IIEF5 = International Index of Erectile Function 5; $VO_{2\ peak}$ = peak oxygen consumption; HGS = handgrip strength.

Table 2. Independent Correlates of Log-Transformed IIEF5 Score.

Variable	β	*p* value
Dependent variable: IIEF5[a] (R^2 = 0.38, $p < .001$)		
Age, years[a]	−0.024	.802
Height, cm	0.126	.108
HbA1c, mg/dl[a]	−0.107	.134
Testosterone, nmol/l[a]	0.095	.157
cfPWV, cm/s[a]	**−0.179**	**.028**
$VO_{2\ peak}$, ml/min/kg[a]	**0.243**	**.004**
Handgrip strength, kg[a]	**0.169**	**.037**

Note. [a]Log transformed. HbA1c = hemoglobin A1c; IIEF5 = International Index of Erectile Function 5; $VO_{2\ peak}$ = peak oxygen consumption.

muscular strength were significantly correlated with male sexual function. Multivariate linear regression analyses showed that aerobic capacity and muscle strength are significantly associated with male sexual function after considering confounders, including age and testosterone. These results suggest that high levels of aerobic capacity and muscle strength may offset aging-induced deterioration of male sexual function. The present findings may provide a novel insight into the role of physical fitness in reducing the risk of ED.

Since the most significant factor of causing ED has been attributed to vascular dysfunctions (Kumagai, Yoshikawa, Myoenzono, et al., 2018; Vlachopoulos, Ioakeimidis, et al., 2008), the association between aerobic fitness and male sexual function may be explained with vascular function. Previously, a lot of studies have demonstrated that aerobic exercise intervention improved vascular functions (Matsubara et al., 2014; Tanahashi et al., 2014; Tanaka et al., 2000; Tomoto et al., 2015). Aerobic exercise increases blood flow and consequently generates the mechanical share in the endothelium, indicating the release of nitric oxide (Hambrecht et al., 2003; Meldrum et al., 2011). Taken together, high aerobic fitness has been suggested to be protective against ED through preferable vascular functions. Aerobic capacity

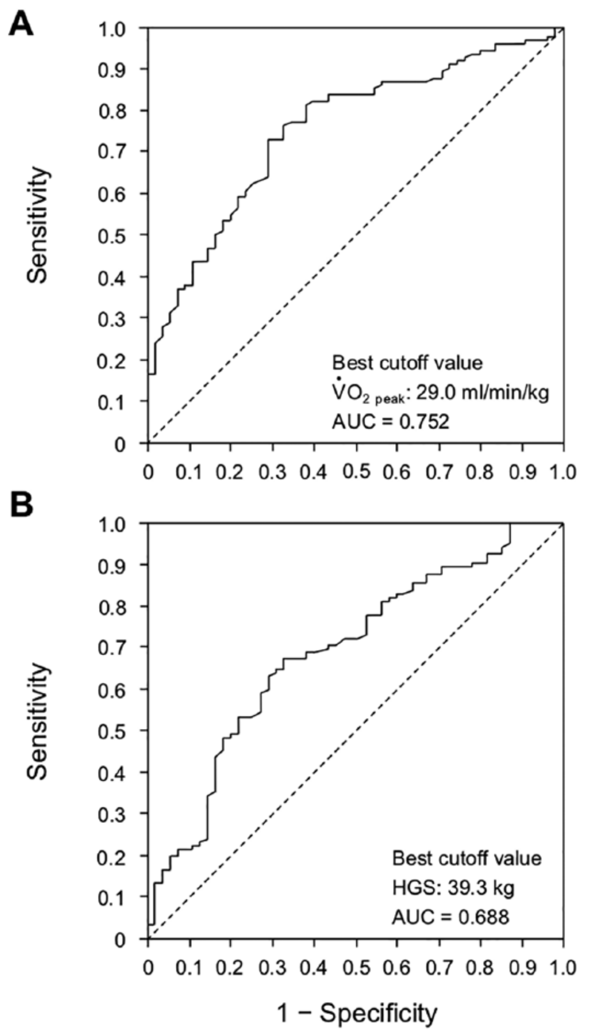

Figure 2. ROC curve of $VO_{2\ peak}$ (A) and HGS (B) for the prediction of ED (IIEF5: less than 22 points).
AUC = area under the curve; ED = erectile dysfunction; HGS = handgrip strength; IIEF5 = International Index of Erectile Function 5; ROC = receiver operator characteristic; $VO_{2\ peak}$ = peak oxygen consumption.

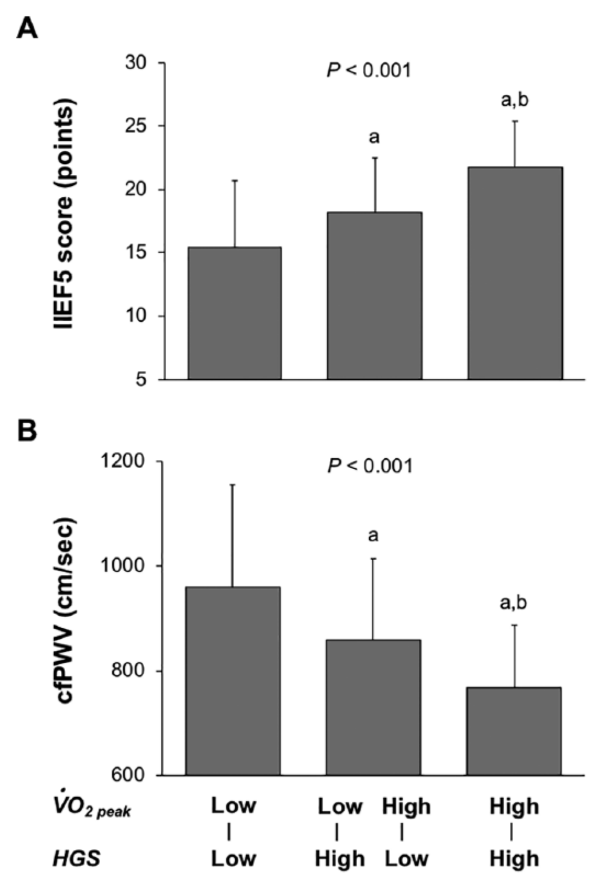

Figure 3. Combined effects of $VO_{2\ peak}$ and HGS on IIEF5 score (A) and cfPWV (B). The participants were stratified based on whether the values of the $VO_{2\ peak}$ and HGS were higher or lower than the cutoff values of $VO_{2\ peak}$ and HGS calculated by ROC analysis. [a]$p < .01$ versus low-$VO_{2\ peak}$ and low-HGS group, [b]$p < .01$ versus low-$VO_{2\ peak}$ and high-HGS group or high-$VO_{2\ peak}$ and low-HGS group. cfPWV = carotid–femoral pulse wave velocity; HGS = handgrip strength; IIEF5 = International Index of Erectile Function 5; ROC = receiver operator characteristic; $VO_{2\ peak}$ = peak oxygen consumption.

was significantly correlated to both male sexual function and arterial stiffness. In addition, aerobic capacity and arterial stiffness were significantly associated with male sexual function after considering age and serum testosterone levels. These results suggest that high physical fitness has a protective effect on aging-induced deterioration of male sexual function through vascular function.

Several studies have previously suggested that muscular strength is associated with cardiovascular morbidity and mortality (Leong et al., 2015; Ortega, Silventoinen, Tynelius, & Rasmussen, 2012; Silventoinen, Magnusson, Tynelius, Batty, & Rasmussen, 2009). Leong et al. (2015) reported that muscular strength assessed by using HGS is a stronger predictor of cardiovascular mortality. Okamoto et al. (2011) have reported that a 10-week, low-intensity resistance training increases muscular strength and improves arterial stiffness and endothelial function. Muscular strength has been suggested to be positively associated with male sexual function through vascular functions. In this study, similar to aerobic capacity, muscular strength was significantly correlated to both male sexual function and arterial stiffness. Furthermore, it was observed that muscular strength and arterial stiffness were significantly associated with male sexual function after considering age and serum testosterone levels. Although previous studies and the present results suggested that high muscular strength has protective effects on male sexual function through vascular functions, the precise mechanism has not been clarified yet. Skeletal muscle has been suggested to produce and release a number of cytokines (myokines), which have protective effects on CVDs (Lee et al., 2015; Zhang, Mu, et al., 2016; Zhang, Song, et al., 2016). Myokines may explain the association between muscular strength and vascular function. Further study is necessary to clarify the relationship between muscular strength and male sexual function.

The present study has several limitations. Since the study design was cross-sectional, the causal relationship between physical fitness and male sexual function was not clarified. A future longitudinal study that includes aerobic or resistance exercise will be necessary to reveal the causal relationship. The present study demonstrated that there was no significant association between serum testosterone levels and IIEF5 score after adjusting for confounders. Previous studies have reported that testosterone was associated with erectile function (Rizk, Kohn, Pastuszak, & Khera, 2017), physical fitness, and/or exercise (Caminiti et al., 2009; Hayes, Herbert, Sculthorpe, & Grace, 2017; Kumagai, Yoshikawa, Zempo-Miyaki, et al., 2018; Kumagai et al., 2016), and cardiovascular function (Akishita et al., 2010; Kumagai et al., 2014, 2015; Vlachopoulos et al., 2014) in men with low testosterone levels. Since the serum testosterone levels in the present subjects were relatively high, it is necessary to confirm the relationship between male sexual function, physical fitness, and cardiovascular function in subjects with low serum testosterone levels.

The present study found that $VO_{2\ peak}$ and HGS were significantly correlated with both male sexual function and arterial stiffness. In addition, multivariate linear regression analyses showed that $VO_{2\ peak}$, HGS, and cfPWV were significantly associated with male sexual function after considering confounders, including age and testosterone. These results suggest that aerobic capacity and muscular strength are associated with male sexual function through vascular function, and high physical fitness may offset the aging-induced deterioration of male sexual function. The present findings may provide a novel insight into the role of physical fitness in reducing the risk of ED and may contribute to establishing a novel treatment approach for ED.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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