

OPEN

Impaired Aerobic Endurance and Muscular Strength in Substance Use Disorder Patients

Implications for Health and Premature Death

Grete Flemmen, MSc and Eivind Wang, PhD

Abstract: Although substance use disorder (SUD) patients are documented to have an inactive lifestyle, which is associated with cardiovascular disease, other lifestyle-related diseases and premature death, evidence regarding their aerobic endurance and muscular strength is limited. Therefore, the authors aimed to evaluate directly assessed maximal oxygen consumption, walking efficiency, as well as maximal strength in a group of SUD patients.

A total of 44 SUD patients in residential treatment, 31 men (31 ± 8 years) and 13 women (34 ± 10 years), were included and completed the physical testing. The patients were compared with an age- and sex-matched reference group.

Male and female SUD patients exhibited a maximal oxygen consumption of 44.6 ± 6.2 and 33.8 ± 6.6 mL \cdot min⁻¹ kg⁻¹, respectively. This was significantly lower than the reference group, 15% ($P = 0.03$) for men and 25% ($P = 0.001$) for women. In addition, the SUD patients had a 13% significantly reduced walking efficiency ($P = 0.02$), compared with healthy controls. The impairments in aerobic endurance were accompanied by significant reductions in maximal strength of 30% ($P = 0.001$) and 33% ($P = 0.01$) for men and women, respectively. In combination, these results imply that SUD patients have impaired endurance and muscular strength compared with what is typically observed in the population, and consequently suffer a higher risk of developing cardiovascular and other lifestyle-related diseases and early death. Effective physical exercise should be advocated as an essential part of the clinical practice of SUD treatment to improve the patient's health and consequently reduce the costs because of the high use of emergency departments, hospital, and medical care.

(*Medicine* 94(44):e1914)

Editor: Jinhai Huo.

Received: June 24, 2015; revised: September 11, 2015; accepted: October 5, 2015.

From the Department of Circulation and Medical Imaging, Faculty of Medicine, the Norwegian University of Science and Technology (GF, EW); and Department of Research and Development, Clinic of Substance Use and Addiction Medicine, St. Olav's University Hospital, Trondheim, Norway (GF); Department of Internal Medicine, University of Utah, Salt Lake City, Utah, USA (EW).

Correspondence: Grete Flemmen, MSc, Department of Circulation and Medical Imaging, Faculty of Medicine, the Norwegian University of Science and Technology, Prinsesse Kristinas gt. 3, 7006 Trondheim, Norway (e-mail: Grete.Flemmen@ntnu.no).

Role of funding Source: This project was funded by the Liaison Committee between the Central Norway Regional Health Authority and the Norwegian University of Science and Technology.

The authors have no conflicts of interest to disclose.

Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.

This is an open access article distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives License 4.0, where it is permissible to download, share and reproduce the work in any medium, provided it is properly cited. The work cannot be changed in any way or used commercially.

ISSN: 0025-7974

DOI: 10.1097/MD.0000000000001914

Abbreviations: HR_{max} = maximal heart rate, ICD-10 = International Classification of Diseases rev 10, [La⁻]_b = lactate concentration in blood, MET = maximal metabolic equivalent, 1RM = one repetition maximum, Q = cardiac output, RER = respiratory exchange ratio, RFD = rate of force development, SUD = substance use disorder, V_E = ventilation, VO_{2max} = maximal oxygen consumption.

INTRODUCTION

Patients with substance use disorder (SUD), classified within International Classification of Diseases rev 10; F10–19 (World Health Organization's classification 1990) have in addition to their mental and behavioral disorders an increased prevalence of cardiovascular disease,¹ cancer,¹ attenuated bone health,² and a decreased life expectancy of 15 to 20 years, the lowest among patients with different mental illnesses.³ Undoubtedly, various causes contribute to the mental as well as physical problems that substance users suffer.³ Evidence, however, is limited regarding the patient groups' physical health status and its likely influence on their overall health problems, cardiovascular system, and muscle strength and function, especially through direct assessment of key factors, such as maximal oxygen consumption (VO_{2max}), walking efficiency, maximal strength, and muscle force development characteristics.

VO_{2max}, commonly also referred to as cardiorespiratory fitness and given in maximal metabolic equivalents (METs), is one of the strongest predictors for mortality from cardiovascular disease and other causes.^{4–6} Analyzing several risk factors, Wei et al⁴ observed that a low VO_{2max} resulted in a similar, if not greater, relative risk of mortality compared with established risk factors, such as diabetes mellitus, high cholesterol levels, hypertension, and cigarette smoking. The relative risk of mortality has been quantified from estimated VO_{2max} showing that a reduction of 1 MET (~ 3.5 mL \cdot min⁻¹ kg⁻¹) corresponded to a 12% increase in mortality.⁵ More recently, this was confirmed by Kodama et al⁶ who observed a decrease of 1 MET to be associated with a 13% to 15% higher risk of all-cause mortality and coronary heart disease.

Not only VO_{2max}, but also skeletal muscle strength has been increasingly recognized as a considerable risk factor for mortality,^{7,8} cardiovascular disease,⁸ and cancer.⁷ The mortality risk from impaired muscle strength is comparable with the elevated risk from hypertension and obesity.⁸ Reduced muscle strength is also shown to result in poor bone health⁹ and an absence of sufficient muscular overload, through lack of physical activity or resistance training, will consequently induce bone loss.¹⁰ Thus, the synergetic effect between muscular strength and VO_{2max} should be emphasized in clinical practice as prevention and treatment of cardiovascular disease as they in combination represent a substantial risk reduction.¹¹

Importantly, both a reduced VO_{2max} and low muscular strength are also shown to be associated with a poor mental health.^{8,12} VO_{2max} is in several studies associated with diagnosis of psychosis or schizophrenia,^{13,14} and a low muscular strength is associated with a 20% to 30% increase in suicide rate in young adults.⁸ The number of suicides in SUD patients may be even higher than in the general young population as a significant part of deaths are because of drug overdose,^{1,3} and it is difficult to determine if this is because of accidents or suicide. Although causality is difficult to interpret from these findings, a low physical fitness typically leads to loss of daily functions, which in turn are associated with depressive symptoms. In contrast, physical activity is documented to be an effective countermeasure.¹⁵

Although documentation of SUD patients' physical health, through direct assessment of VO_{2max} and muscular strength is limited, a few studies are indicating that the patient group is indeed at risk. Recent research has evaluated the effects of aerobic endurance training and shown that SUD patients had a ~20% lower VO_{2max} than what is typically seen in the population.¹⁶ Our results were in line with observations from methamphetamine dependents, revealing severely reduced VO_{2max} values,¹⁷ and SUD patients in a rehabilitation project, which displayed values of 39 ± 10 (men) and 31 ± 8 (women) $mL \cdot min^{-1} kg^{-1}$ in ~30-year-old patients.¹⁸ Although it lacks a comparison with healthy individuals, one recent study¹⁷ documented that SUD patients' reduced VO_{2max} may be accompanied by reductions in maximal muscle strength with reported values as low as ~60 kg in leg press and ~40 kg in chest press. It, however, is difficult to interpret these findings because joint angle are not reported and apparatus construction is not known, and these factors are clearly relevant for comparison with other populations. Despite that, muscular strength reductions often accompany inactivity-related reductions in VO_{2max} ; this is to our knowledge the only study that has indicated that SUD patients may have an impaired muscular strength.

Although a few studies imply that SUD patients may be at risk for cardiovascular disease, other lifestyle-related diseases and premature death because of their reduced cardiorespiratory and muscular fitness, there is a clear need for a more robust assessment of the SUD patients' physical health across sex, age, and primary drug dependence. Therefore, the aim of this study was to directly assess the patients' muscular strength as well as aerobic endurance. Specifically, our hypothesis was that SUD patients had a significantly reduced VO_{2max} , walking efficiency, maximal muscle strength, and muscle rate of force development (RFD) compared with an age- and sex-matched control group.

METHODS

Patients

We included 44 patients, 13 women (age 34 ± 10 years; weight 80.0 ± 20.3 kg; and height 165 ± 6 cm) and 31 males (age 31 ± 8 years; weight 85.1 ± 15.9 kg; and height 181 ± 7 cm), with a diagnosis of SUD; International Classification of Diseases rev 10: F10–F19 (mental and behavioral disorders because of psychoactive substance use). Twenty-two of the men and 9 of the women were current smokers, respectively. Patients' medical use is given in Table 1. Patients were all in a ~3 months' full-time residential treatment program. All patients agreed voluntarily to participate in the study and signed a written informed consent. Patients were excluded if they had been abstinent from drugs for the last 6 months or if they had

TABLE 1. Substance Use Disorder Patients' Drug Use and Prescribed Medicine

	Man (n = 31)	Woman (n = 13)
Primary Drug		
Heroin	2	—
Benzodiazepines, Sed, hypnotic	1	1
Amphetamine	20	10
Cannabis	8	2
Secondary Drug		
Alcohol	1	3
Heroin	5	1
Opiates, painkillers	4	—
Cocaine	2	—
Amphetamine	4	1
Cannabis	14	8
Hallucinogens	1	—
Prescribed Medicines for Symptoms		
Attention deficit hyperactivity disorder	3	2
Allergies	4	4
Anxiety	4	2
Arthritis	4	1
Asthma/chronic obstructive pulmonary disease	4	2
Depression	5	2
Epilepsy	6	1
Hypertension	3	1
Infections	1	3
Schizophrenia/bipolar	9	5
Skin disorder	2	2
Substitutional treatment	4	2
Other	8	3

Data are presented as mean \pm SD. Prescribed medicines in substitutional treatment are methadone and suboxone. Other prescribed medicines: skin disorder, pain, and inflammation. Sed = sedatives.

impairments or injuries that prevented them from completing the treadmill and/or strength tests. All patients who fulfilled the inclusion criteria who arrived in the treatment clinic in a 6 months period were included in the study. The patients' physical performance was compared with a healthy age- and sex-matched reference group, targeted to exhibit what is typically observed in the population, consisting of 14 women (age 34 ± 8 years; weight 68.8 ± 7.9 kg; and height 171 ± 5 cm) and 11 men (age 37 ± 9 years; weight 89.3 ± 10.9 kg; and height 183 ± 6 cm), recruited among students and employees at the local University Hospital. A total of 20% of the controls (one of the men and 4 of the women, respectively) were current smokers. The regional medical ethics committee approved the study and it was carried out in accordance with the Helsinki Declaration.

Testing Procedures

Maximal Oxygen Consumption and Walking Efficiency

After a warm-up period of 10 minutes, patients started the 5 minutes walking efficiency test at 5% inclination and $4.5 km \cdot h^{-1}$. Oxygen consumption was obtained every 10 seconds (Metamax II Cortex Biophysik GmbH, Leipzig,

Germany), and net walking efficiency was calculated as an average of the last minute as

$$\text{Net walking efficiency} = \frac{\text{External work accomplished (Kcal}\cdot\text{min}^{-1})}{\text{Energy expenditure (Kcal}\cdot\text{min}^{-1})} \cdot 100$$

where oxygen consumption and work both were expressed as kcal to express walking percentage efficiency.¹⁹ Continuously from the walking efficiency test, the patients progressed to the VO_{2max} test, which consisted of an incremental ramped protocol till exhaustion, where velocity was increased by 1 km·h⁻¹ every minute and inclination kept constant at 5%. Maximal oxygen consumption was calculated as an average of the highest 30-second window. Pulmonary ventilation and respiratory exchange ratio were averaged in the same period as the VO_{2max}. Criteria for reaching VO_{2max} were used in accordance with previous literature.²⁰ Heart rate measurements were obtained using heart rate monitors (Polar Electro, Finland), and maximal heart rate was estimated as 3 to 5 beats·min⁻¹ added to the highest heart rate during the last minute.²⁰ After completion of the VO_{2max} test, a fingertip blood sample was taken for measurements of lactate concentration in blood (Biosen C_line, EKF Diagnostics GmbH, Barleben, Germany).

Maximal Strength and Rate of Force Development Measurements

After 2 warm-up sets, one repetition maximum (1RM) was performed in a hack squat machine (Impulse Fitness IT7006, Shandong, China). The patients started in a standing position and then moved eccentrically down to a 90° knee angle position. After a fraction of a second stop, the patient then moved concentrically with a fast intended velocity. The correct knee angle position was assessed with a goniometer. The load was increased with increments of 10 kg, and 1RM was achieved within 4 to 8 lifts. The patients had rest periods of 4 minutes between their attempts. After completion of the 1RM test, RFD was measured using a force plate (9286AA, Kistler, Switzerland) in the same apparatus with a weight corresponding to 75% of 1RM. Measurements were obtained with a 2000 Hz frequency (Bioware v3.06b, Kistler, Switzerland). As for the 1RM test, the patients were instructed to try and lift the weight as fast as possible in the concentric movement. The highest RFD among 3 attempts was used for the data analysis, and patients had 3 minutes rest periods between their attempts.

Statistical Analysis

Statistical analyses were performed using the SPSS, version 20, software program (Chicago, IL), and figures were made using the software GraphPad Prism 5 (San Diego, CA). Independent samples *t* test were used to compare differences between the SUD patient group and the reference group. Correlations between primary substance use, sex, age, substance use history, and physical capacity were analyzed using linear Pearson correlation regression analysis. Results were considered statistically significant at a 2-tailed level of *P* < 0.05. Data are presented as mean ± SD unless otherwise stated.

RESULTS

All 44 SUD patients [21–30 years (n = 23); 31–40 years (n = 14); and 41–50 years (n = 7)] in residential treatment and the 25 control age- and sex-matched patients [21–30 years (n = 10); 31–40 years (n = 7); and 41–50 years (n = 8)] completed the VO_{2max} test, walking efficiency test, and strength tests. No differences were observed in body mass between the 2 groups, but female SUD patients tended (*P* = 0.08) to be heavier than the controls.

Aerobic Endurance

Maximal oxygen consumption was significantly lower in SUD patients compared with the reference group (Table 2), this was apparent for both sexes (Fig. 1A). Women and men displayed reductions of 25% (*P* = 0.001) and 15% (*P* = 0.03), respectively. The lower aerobic power was consistently present in all age groups (Fig. 1B). No significant differences were observed between patients who had amphetamine (n = 30) or cannabis (n = 10) as their primary drug (Fig. 2). Maximal oxygen consumption correlated significantly with years of drug use; however, this correlation was not present when it was adjusted for age.

As for the maximal aerobic power, the SUD patients' aerobic endurance at a submaximal level below anaerobic threshold was also impaired. No differences were observed between women and men in walking efficiency and as a consequence, data were collapsed (Table 3; Fig. 3). The impairment was apparent as a 12% (*P* = 0.05) higher oxygen cost of walking at 4.5 km/h at 5% inclination (Fig. 3A), and this was mirrored by a 13% (*P* = 0.02) reduction in walking efficiency (Fig. 3B). This was further accompanied by a significant increase in ventilation (*P* = 0.042) and respiratory exchange

TABLE 2. Physiological Variables Measured During a Maximal Oxygen Uptake Test

	SUD Patients (n = 44)		Reference Group (n = 25)	
	Male (n = 31)	Female (n = 13)	Male (n = 11)	Female (n = 13)
VO _{2max} , L·min ⁻¹	3.74 ± 0.62**	2.60 ± 0.35**	4.56 ± 0.44	3.10 ± 0.31
VE, L·min ⁻¹	113.6 ± 19.5*	77.4 ± 13.7**	131.5 ± 17.5	95.9 ± 11.5
RER	1.15 ± 0.07	1.13 ± 0.07	1.13 ± 0.04	1.11 ± 0.03
HR _{max} , beat·min ⁻¹	185 ± 10	181 ± 13*	192 ± 11	190 ± 10
[La] _b , mM	9.98 ± 2.8	7.37 ± 2.12*	12.03 ± 3.23	8.82 ± 1.31

Data are presented as mean ± SD. HR_{max} = maximal heart rate, [La]_b = lactate concentration in blood, RER = respiratory exchange ratio, SUD = substance use disorder; VE = ventilation, VO_{2max} = maximal oxygen uptake.

* *P* < 0.05.

** *P* < 0.01. Significant differences between patient group and reference group.

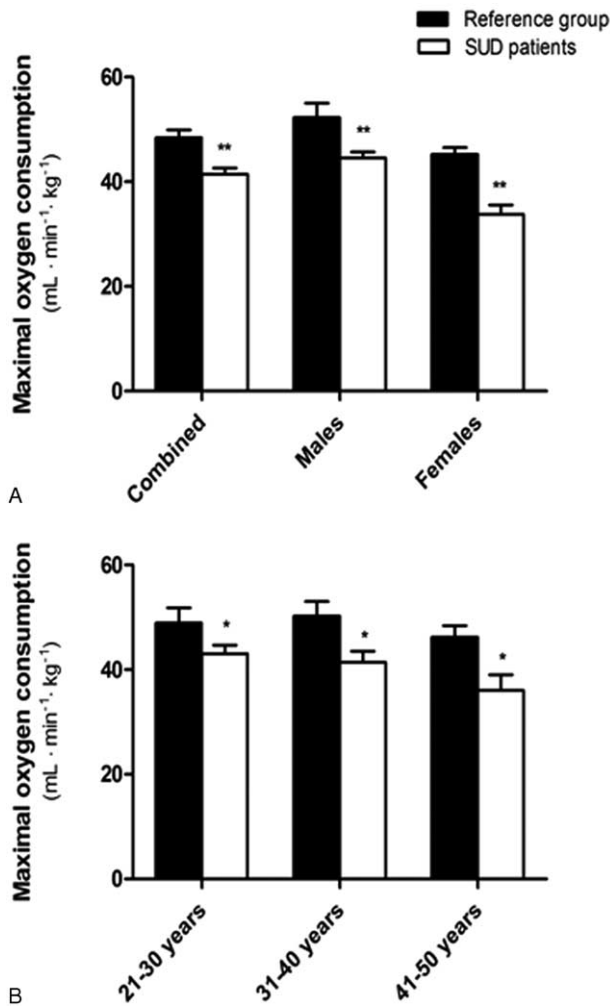


FIGURE 1. A, Substance use disorder patients' maximal oxygen consumption were compared with the reference group, both sexes and combined. Data are presented as mean ± SE. **Significant difference between the reference group and SUD patients ($P < 0.01$). B, Maximal oxygen consumption, comparing SUD patients and reference group, all age groups. Data are presented as mean ± SE. *Significant difference between the groups ($P < 0.05$). SUD = substance use disorder.

ratio ($P = 0.001$) among the SUD patients. Systematically, the impairments were exhibited in both women and men and across age.

Muscular Strength

Substance use disorder patients had a significantly lower maximal muscle strength compared with the reference group, with 1RM reductions of 30% ($P = 0.001$) and 33% ($P = 0.010$) in men and women, respectively (Fig. 4A). A significant $r = 0.36$ correlation between 1RM and RFD was observed ($y = 4.0x + 874$; 95% confidence interval: 1.4–6.5 and 555–1193; $P < 0.01$), and the reductions in 1RM were accompanied by a clear tendency toward a reduced RFD (Fig. 4B), expressing 20% and 15% reductions in men and women, respectively, compared with healthy controls. Because an association between muscular strength and walking efficiency, has been

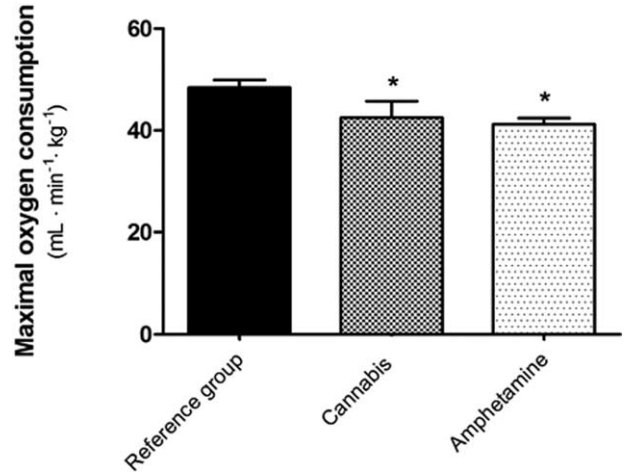


FIGURE 2. Maximal oxygen consumption in patients with amphetamine or cannabis as their primary drug, was compared with reference group. Data are presented as mean ± SE. *Significant difference between the groups ($P < 0.05$). No significant differences between the 2 drug categories.

established previously, the strength parameters and walking efficiency were tested against each other, revealing that the RFD significantly correlated ($r = 0.38$) with walking efficiency ($y = 0.0037x + 17.9$; 95% confidence interval: 0.0013–0.0062 and 14.3–21.4; $P < 0.01$), whereas 1RM did not. Furthermore, the differences in maximal strength and RFD between SUD patients and the reference group were consistently present for all age groups, but were not affected by the drug type dependency.

DISCUSSION

Because VO_{2max} and muscular strength are strong predictors for physical and mental health, but evidence of directly assessed aerobic endurance and strength components rarely has been presented, our aim was to present such components and evaluate their implications for health in SUD patients. The main findings of the current study were that SUD patients have a reduced VO_{2max} compared with what is typically observed in the population; aerobic endurance is further reduced because of reductions in walking efficiency; the aerobic endurance impairments were accompanied by reduced maximal strength and ability to perform rapid muscle contractions; and the

TABLE 3. Walking Economy at 4.5 km/h, 5% Inclination on a Treadmill

	SUD Patients (n = 44)	Reference Group (n = 25)
VO_2 , mL · min ⁻¹ · kg ⁻¹	19.1 ± 1.6*	18.0 ± 1.6
VE, L · min ⁻¹	36.4 ± 7.6*	32.2 ± 6.5
RER	0.91 ± 0.04**	0.87 ± 0.04
%HR _{max}	64 ± 8	61 ± 8

Data are presented as mean ± SD. %HR_{max} = percentage of maximal heart rate, RER = respiratory exchange ratio, SUD = substance use disorder, VE = ventilation, VO_2 = oxygen uptake.

* $P < 0.05$.

** $P < 0.01$. Significant differences between patient group and reference group.

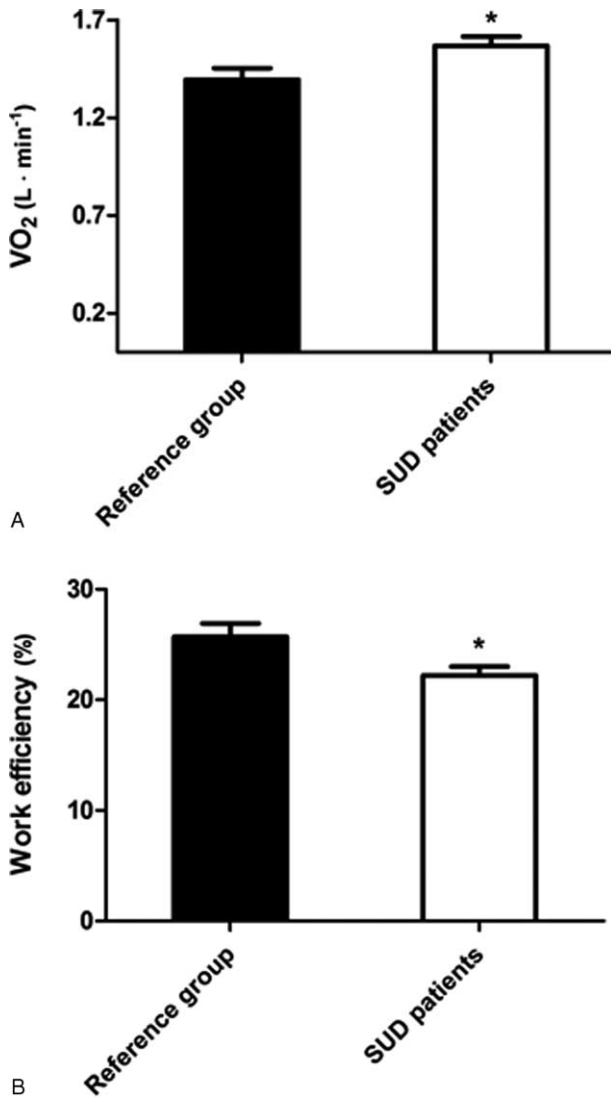


FIGURE 3. A, Oxygen cost of walking at 4.5 km·h⁻¹ at 5% inclination on the treadmill, comparing reference group with substance use disorder patients. Data are presented as mean ± SE. *Significant difference between the groups ($P < 0.05$). B, Walking efficiency at 4.5 km/h at 5% inclination on the treadmill, comparing reference group with substance use disorder patients. Data are presented as mean ± SE. *Significant difference between the groups ($P < 0.05$).

impairments in aerobic endurance and muscular strength were systematically present across age, sex, primary drug, and history of substance use. In combination, these findings imply that SUD patients indeed are at risk for developing cardiovascular disease, cancer, attenuated bone health, and premature death, and that inactivity may be responsible, at least in part, for the physical health reductions.

Maximal Oxygen Consumption and Substance Use Disorder

Substance use disorder patients in the current study exhibited a systematically reduced VO_{2max} compared with healthy

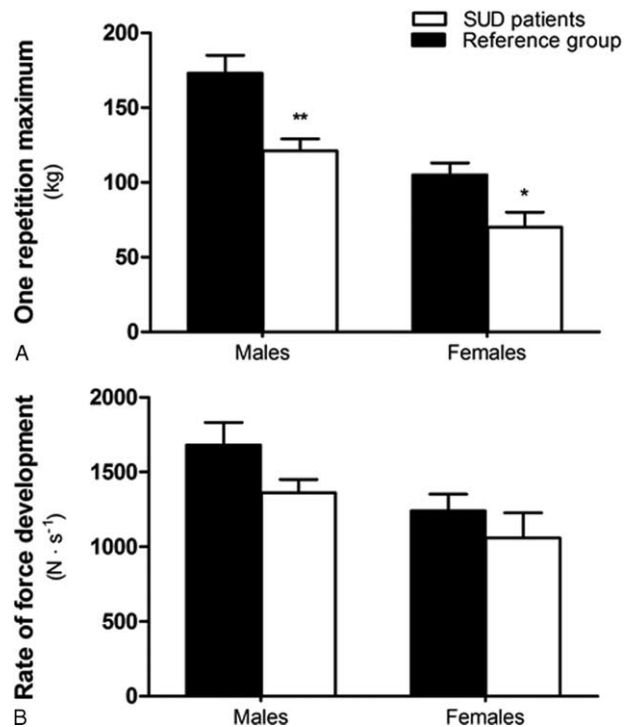


FIGURE 4. A, Muscular strength (one repetition maximum) in substance use disorder patients and reference group. Data are presented as mean ± SE. *Significant difference between the groups ($P < 0.05$) and **($P < 0.01$). B, Rate of force development in substance use disorder patients and reference group. Data are presented as mean ± SE.

controls. The values of the patients in this study are also below what recently was reported as reference data for the Norwegian population.²¹ Specifically, the women in our study showed a large attenuation in aerobic power, equivalent to what is observed with ~25 years of aging,²² and associated with a ~25% increased risk of mortality.^{5,6} The reduction in VO_{2max} was not related to the patients' drug type dependency (Fig. 2), and was present for all age groups (Fig. 1B). Although well below what is typically observed in the population, our VO_{2max} results are somewhat higher than previous studies that have observed values of 39 (men) and 31 (women) mL · min⁻¹ kg⁻¹,¹⁸ 32 (indirectly estimated for men and women combined) mL · min⁻¹ kg⁻¹,²³ and 31 (men) and 23 (women) mL · min⁻¹ kg⁻¹.¹⁷ The discrepancy between these results may be because of the different populations tested, indirect or direct measurements of oxygen uptake, testing modality (i.e., bicycle or treadmill), and protocol. In combination, our study and previous studies are in agreement, observing that SUD patients, however, have a reduced VO_{2max}, and thus have an elevated risk for cardiovascular disease, other lifestyle-related diseases and premature death. Alterations in VO_{2max} is suggested to primarily be caused by changes in cardiac output and function,²⁴ and a causality has been shown both with training²⁵ and detraining.²⁶ This implies that the very low VO_{2max} that is observed in SUD patients is likely accompanied by a severely reduced cardiac output, and that this may be one of the factors that can explain the high prevalence of cardiovascular disease within the patient group.

Walking Efficiency

Contributing to an overall reduced aerobic endurance in SUD patients in the current study was also a reduction in walking efficiency. Walking efficiency is approximately 25% in healthy individuals,²⁷ and our observation of 26% among the healthy controls was in line with this. In contrast, the SUD patients exhibited a 13% lower efficiency, meaning that not only do they have to work on a higher percentage of their VO_{2max} when carrying out daily tasks, but they also have to do the certain amount of work with a larger cost of energy compared with healthy individuals. This is adding weight to an already challenging situation and certainly contributes to the negative spiral toward even more inactivity, and an aggravation of the calamitous lifestyle. The decreased walking efficiency has to our knowledge not been documented in SUD patients before, and was present for both men and women in all age groups (Fig. 3). Thought provoking, their walking efficiency is similar to an efficiency that is observed among 50-year-old men and women.²⁸ Again, as for the VO_{2max} measurements, the reduced efficiency was not associated with the substance use history or drug type dependency, and advocates that the SUD patients' lifestyle, and absence of sufficient activity, may be the explanation for their weakened aerobic energy production.

Maximal Muscle Strength, Force Development Characteristics and Substance Use Disorder Patients

In addition to endurance, skeletal muscle strength is important for the assessment of an individuals' physical health. The current study show that SUD patients exhibited significant maximal strength reductions compared with the healthy controls. Although strength training has previously been applied on SUD patients in residential treatment,¹⁷ it has, to our knowledge, not been known how their strength relates to what is observed in healthy patients. The 33% (men) and 30% (man) reduced strength in SUD patients in our study corresponds to what is observed with 30 to 40 years of aging,²⁹ and puts the patients at an elevated risk for falls and fractures,³⁰ premature death,^{8,31} and possibly cancer.³¹ Importantly, reductions in maximal strength are usually accompanied by reductions in muscle RFD.^{19,32} Therefore, it was not surprising that in the current study, RFD was correlated with 1RM. Rate of force development may be an even more important predictor for physical function³⁰ compared with maximal strength because it is more related to functional tasks, balance adjustments, and prevention of falls, where the time to reach maximal strength is limited. The 15% to 20% lower RFD among the SUD patients in this study may contribute to more challenging everyday situations and risk of injuries.

A relationship between muscular strength and aerobic endurance has also been established, specifically through the effects of RFD on aerobic work and walking efficiency.^{33,34} It is suggested that alterations in RFD will lead to changes in the force-velocity curve,³³ resulting in changes in oxygen demand in the working muscle, and consequently changes in blood flow.³⁴ Indeed, a correlation between RFD and walking efficiency was documented in this study, and it is likely that a poor RFD in the SUD patients have resulted in a worsening of their aerobic endurance in accordance with previous literature.^{19,32}

Physical Health in Substance Use Disorder Patients: Implications for Mental Health

Previously, both VO_{2max} and muscular strength have been observed to be predictors for mental health.^{8,12} A weakened

aerobic endurance has been associated with depression¹² and psychosis,¹³ whereas muscular strength have been associated with psychiatric diagnoses and even suicide.⁸ Although it is often difficult to establish a cause-effect relationship, it has been demonstrated that aerobic endurance training can decrease depression.¹⁶ Enhanced physical health may lead to an improved mental health because of changes in the individual's perception of physical as well as social factors. Because SUD patients in the current study display large reductions in both endurance and muscular capacity and function, it is likely that this is associated with their mental health. It is an interesting topic of future research if effective physical training may be able to improve their mental state, and thus ultimately also have an effect on their substance use.

Reduced Physical Health in Substance Use Disorder Patients: Clinical Treatment Perspectives

Although the sample size in the current study is relatively small, our results indicate that SUD patients have a reduced aerobic endurance and muscular strength, consequently putting them at risk for diseases, premature death, and an aggravation of their mental health. The SUD patients' attenuated physical health likely has multifactorial causes. Drug use and cigarette smoking may directly have contributed to the reduced physical health observed in the current study. Indeed, especially cigarette smoking is well documented to effect cardiorespiratory function and consequently reduce exercise capacity^{35,36} as well as increase the risk of cardiorespiratory diseases.³⁷ In addition, the patient groups' inactivity-related lifestyle may indirectly have affected their aerobic endurance and muscular strength as the lack of activity previously has been shown to dramatically reduce both aerobic endurance²⁶ and muscular strength.³⁸ Exercise training is shown to work as an effective countermeasure for reduced endurance and strength, and should be emphasized as a part of the clinical treatment. Although today's treatment of SUD patients commonly includes physical activity, it appears random and unstructured, without the sufficient training intensity to have a robust effect.¹⁶ Importantly, high intensity is favorable to yield the most optimal effects both for endurance²⁵ and muscular strength,³⁹ and documented to be feasible and effective also for untrained patient populations.^{16,32} Therefore, as one element to counteract the SUD patients from spiraling down the physical and mental cascade toward more inactivity and substance dependence, effective training for improving aerobic endurance, muscular strength, and function should be applied in the clinics, preferably targeting the optimal exercise intensity and modality.

CONCLUSIONS

Applying direct assessment of physiological variables, our findings show that SUD patients have a reduced VO_{2max} , walking efficiency, maximal strength, and ability to rapid force development compared with healthy individuals. Because reductions in these physiological factors are associated with an elevated risk of cardiovascular disease, cancer, poor bone quality, premature death, and mental health, effective exercise training should be a part of the clinical treatment of the patient group. This may not only have a beneficial effect on the patients' physical and mental health, but could also reduce socioeconomic costs.

REFERENCES

1. Stenbacka M, Leifman A, Romelsjo A. Mortality and cause of death among 1705 illicit drug users: a 37 year follow up. *Drug Alcohol Rev.* 2010;29:21–27.
2. Kim EY, Kwon do H, Lee BD, et al. Frequency of osteoporosis in 46 men with methamphetamine abuse hospitalized in a National Hospital. *Forensic Sci Int.* 2009;188:75–80.
3. Nordentoft M, Wahlbeck K, Hallgren J, et al. Excess mortality, causes of death and life expectancy in 270,770 patients with recent onset of mental disorders in Denmark, Finland and Sweden. *PLoS One.* 2013;8:e55176.
4. Wei M, Kampert JB, Barlow CE, et al. Relationship between low cardiorespiratory fitness and mortality in normal-weight, overweight, and obese men. *J Am Med Assoc.* 1999;282:1547–1553.
5. Myers J, Prakash M, Froelicher V, et al. Exercise capacity and mortality among men referred for exercise testing. *N Engl J Med.* 2002;346:793–801.
6. Kodama S, Saito K, Tanaka S, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. *J Am Med Assoc.* 2009;301:2024–2035.
7. Ruiz JR, Sui X, Lobelo F, et al. Association between muscular strength and mortality in men: prospective cohort study. *Br Med J.* 2008;337:a439.
8. Ortega FB, Silventoinen K, Tynelius P, et al. Muscular strength in male adolescents and premature death: cohort study of one million participants. *Br Med J.* 2012;345:e7279.
9. Cussler EC, Lohman TG, Going SB, et al. Weight lifted in strength training predicts bone change in postmenopausal women. *Med Sci Sports Exerc.* 2003;35:10–17.
10. Kohrt WM, Barry DW, Schwartz RS. Muscle forces or gravity: what predominates mechanical loading on bone? *Med Sci Sports Exerc.* 2009;41:2050–2055.
11. Artero EG, Lee DC, Lavie CJ, et al. Effects of muscular strength on cardiovascular risk factors and prognosis. *J Cardiopulm Rehabil Prev.* 2012;32:351–358.
12. Galper DI, Trivedi MH, Barlow CE, et al. Inverse association between physical inactivity and mental health in men and women. *Med Sci Sports Exerc.* 2006;38:173–178.
13. Koivukangas J, Tammelin T, Kaakinen M, et al. Physical activity and fitness in adolescents at risk for psychosis within the Northern Finland 1986 Birth Cohort. *Schizophr Res.* 2010;116:152–158.
14. Heggelund J, Nilsberg GE, Hoff J, et al. Effects of high aerobic intensity training in patients with schizophrenia: a controlled trial. *Nord J Psychiatry.* 2011;65:269–275.
15. Brown RA, Abrantes AM, Read JP, et al. Aerobic exercise for alcohol recovery: rationale, program description, and preliminary findings. *Behav Modif.* 2009;33:220–249.
16. Flemmen G, Unhjem R, Wang E. High-intensity interval training in patients with substance use disorder. *Biomed Res Int.* 2014;2014:616935.
17. Dolezal BA, Chudzynski J, Storer TW, et al. Eight weeks of exercise training improves fitness measures in methamphetamine-dependent individuals in residential treatment. *J Addict Med.* 2013;7:122–128.
18. Mamen A, Martinsen EW. The aerobic fitness of substance abusers voluntarily participating in a rehabilitation project. *J Sports Med Phys Fitness.* 2009;49:187–193.
19. Hoff J, Tjonna AE, Steinshamn S, et al. Maximal strength training of the legs in COPD: a therapy for mechanical inefficiency. *Med Sci Sports Exerc.* 2007;39:220–226.
20. Wang E, Solli GS, Nyberg SK, et al. Stroke volume does not plateau in female endurance athletes. *Int J Sports Med.* 2012;33:734–739.
21. Edvardsen E, Scient C, Hansen BH, et al. Reference values for cardiorespiratory response and fitness on the treadmill in a 20- to 85-year-old population. *Chest.* 2013;144:241–248.
22. Fleg JL, Morrell CH, Bos AG, et al. Accelerated longitudinal decline of aerobic capacity in healthy older adults. *Circulation.* 2005;112:674–682.
23. Roessler KK. Exercise treatment for drug abuse: a Danish pilot study. *Scand J Public Health.* 2010;38:664–669.
24. Saltin B, Calbet JA. Point: in health and in a normoxic environment, VO₂ max is limited primarily by cardiac output and locomotor muscle blood flow. *J Appl Physiol.* 2006;100:744–745.
25. Helgerud J, Hoydal K, Wang E, et al. Aerobic high-intensity intervals improve VO₂max more than moderate training. *Med Sci Sports Exerc.* 2007;39:665–671.
26. Saltin B, Blomqvist G, Mitchell JH, et al. Response to exercise after bed rest and after training. *Circulation.* 1968;38:VIII–VII78.
27. Hoydal KL, Helgerud J, Karlsen T, et al. Patients with coronary artery- or chronic obstructive pulmonary disease walk with mechanical inefficiency. *Scand Cardiovasc J.* 2007;41:405–410.
28. Mian OS, Thom JM, Ardigo LP, et al. Metabolic cost, mechanical work, and efficiency during walking in young and older men. *Acta Physiol.* 2006;186:127–139.
29. Lindle RS, Metter EJ, Lynch NA, et al. Age and gender comparisons of muscle strength in 654 women and men aged 20–93 yr. *J Appl Physiol.* 1997;83:1581–1587.
30. Aagaard P, Simonsen EB, Andersen JL, et al. Increased rate of force development and neural drive of human skeletal muscle following resistance training. *J Appl Physiol.* 2002;93:1318–1326.
31. Ruiz JR, Sui X, Lobelo F, et al. Muscular strength and adiposity as predictors of adulthood cancer mortality in men. *Cancer Epidemiol Biomarkers Prev.* 2009;18:1468–1476.
32. Wang E, Helgerud J, Loe H, et al. Maximal strength training improves walking performance in peripheral arterial disease patients. *Scand J Med Sci Sports.* 2010;20:764–770.
33. Osteras H, Helgerud J, Hoff J. Maximal strength-training effects on force-velocity and force-power relationships explain increases in aerobic performance in humans. *Eur J Appl Physiol.* 2002;88:255–263.
34. Barrett-O’Keefe Z, Helgerud J, Wagner PD, et al. Maximal strength training and increased work efficiency: contribution from the trained muscle bed. *J Appl Physiol.* 2012;113:1846–1851.
35. Cooper KH, Gey GO, Bottenberg RA. Effects of cigarette smoking on endurance performance. *J Am Med Assoc.* 1968;203:189–192.
36. Chatterjee S, Dey SK, Nag SK. Maximum oxygen uptake capacity of smokers of different age groups. *Jpn J Physiol.* 1987;37:837–850.
37. Ockene IS, Miller NH. Cigarette smoking, cardiovascular disease, and stroke: a statement for healthcare professionals from the American Heart Association. American Heart Association Task Force on Risk Reduction. *Circulation.* 1997;96:3243–3247.
38. Narici MV, Roi GS, Landoni L, et al. Changes in force, cross-sectional area and neural activation during strength training and detraining of the human quadriceps. *Eur J Appl Physiol Occup Physiol.* 1989;59:310–319.
39. Heggelund J, Fimland MS, Helgerud J, et al. Maximal strength training improves work economy, rate of force development and maximal strength more than conventional strength training. *Eur J Appl Physiol.* 2013;113:1565–1573.