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Reduced peak oxygen uptake and implications for cardiovascular health and quality of life in patients with schizophrenia

Jørn Heggelund[1,2,3*], Jan Hoff[4,5†], Jan Helgerud[4,6,7†], Geir E Nilsberg[3†] and Gunnar Morken[1,3†]

Abstract

Background: Peak oxygen uptake (VO_{2peak}) is a strong predictor of cardiovascular disease (CVD) and all-cause mortality, but is inadequately described in patients with schizophrenia. The aim of this study was to evaluate treadmill VO_{2peak}, CVD risk factors and quality of life (QOL) in patients with schizophrenia (ICD-10, F20-29).

Methods: 33 patients, 22 men (33.7 ± 10.4 years) and 11 women (35.9 ± 11.5 years), were included. Patients VO_{2peak} were compared with normative VO_{2peak} in healthy individuals from the Nord-Trøndelag Health Study (HUNT). Risk factors were compared above and below the VO_{2peak} thresholds; 44.2 and 35.1 $ml \cdot kg^{-1} \cdot min^{-1}$ in men and women, respectively.

Results: VO_{2peak} was 37.1 ± 9.2 $ml \cdot kg^{-1} \cdot min^{-1}$ in men with schizophrenia; 74 ± 19% of normative healthy men ($p < 0.001$). VO_{2peak} was 35.6 ± 10.7 $ml \cdot kg^{-1} \cdot min^{-1}$ in women with schizophrenia; 89 ± 25% of normative healthy women (n.s.). Based on odds ratio patients were 28.3 (95% CI = 1.6-505.6) times more likely to have one or more CVD risk factors if they were below the VO_{2peak} thresholds. VO_{2peak} correlated with the SF-36 physical functioning ($r = 0.58$), general health ($r = 0.53$), vitality ($r = 0.47$), social function ($r = 0.41$) and physical component score ($r = 0.51$).

Conclusion: Men with schizophrenia have lower VO_{2peak} than the general population. Patients with the lowest VO_{2peak} have higher odds of having one or more risk factors for cardiovascular disease. VO_{2peak} should be regarded as least as important as the conventional risk factors for CVD and evaluation of VO_{2peak} should be incorporated in clinical practice.

Background

Patients suffering from schizophrenia have a mortality risk that is two to three times that of the general population and the leading cause of death is cardiovascular disease (CVD) [1,2]. Although, multifactor causes have been identified, reduced cardiorespiratory fitness has probably been overlooked as a risk factor for CVD in patients with schizophrenia [3].

Cardiorespiratory fitness, measured as peak oxygen uptake (VO_{2peak}) is a strong predictor of CVD and all-cause mortality [4,5]. Improvements in VO_{2peak} have indicated reduced risk of CVD, coronary heart disease and all cause mortality [5]. VO_{2peak} is often a stronger predictor of mortality than conventional risk factors for CVD [6]. McAuley and Blair [7] recently pointed out reduced cardiorespiratory fitness as a greater health threat than obesity and suggested that more emphasis should be put on increasing VO_{2peak}. This might be especially important considering that higher levels of VO_{2peak} seems to attenuate or eliminate the increased health risk associated with obesity [8]. Findings from the epidemiological Nord-Trøndelag Health Study (the HUNT Study) demonstrate that physical active people with a clustering of cardiovascular risk factors appears to have comparable risk of premature death as inactive individuals without risk factors [9]. In the same cohort men with VO_{2peak} below 44.2 $ml \cdot kg^{-1} \cdot min^{-1}$ were eight times more likely to have a cluster of CVD risk factors, compared to men above 50.5 $ml \cdot kg^{-1} \cdot min^{-1}$ [10].

Results from the Aerobics Center Longitudional Study further suggest that people with low VO_{2peak} is

* Correspondence: Jorn.Heggelund@ntnu.no
† Contributed equally
[1]Norwegian University of Science and Technology, Faculty of Medicine, Department of Neuroscience, Trondheim, Norway
Full list of author information is available at the end of the article

characterized by depressive symptoms and low emotional well being [11]. High levels of VO_{2peak} are associated with high levels of quality of life (QOL) [12]. Body mass index (BMI) are found inversely related to QOL in patients with schizophrenia [3] but the relation between VO_{2peak} and perceived QOL are not evaluated.

Objective measures of VO_{2peak} have rarely been presented in patients with schizophrenia. The classical study by Carlson et al. [13] were the first to describe oxygen uptake in patients with schizophrenia, but many of their patients did not reach values close to maximal oxygen uptake. Our research group revealed significant changes in VO_{2peak} after eight weeks of high aerobic intensity training in patients with schizophrenia [14]. Recently, Strassnig et al. [3] published measures of oxygen uptake in 117 patients with schizophrenia that were exceedingly low (4.4 metabolic equivalents ≈ 15.4 $ml \cdot kg^{-1} \cdot min^{-1}$). This VO_{2peak} value are much lower than the VO_2 required for walking in patients with schizophrenia [14], and at a level that may indicate a need for heart transplant in heart failure patients [15].

The primary aim of this study was to evaluate objectively measured VO_{2peak} during walking or running in men and women with schizophrenia compared to VO_{2peak} in healthy individuals from the Nord-Trøndelag Health Study (HUNT). We hypothesized that patients with schizophrenia had reduced VO_{2peak} compared to normative healthy individuals. The secondary aim was to evaluate relationships between VO_{2peak}, risk factors for cardiovascular disease, and quality of life.

Methods

Subjects

We included 33 patients, 11 women and 22 men, with ICD-10 schizophrenia, schizotypal or delusional disorders (F20 to F29) in the study. Patients were in- and out-patients at a University hospital and had agreed to take part in exercise interventions studies. All patients were under antipsychotic medical treatment. 24 patients were smokers. Exclusion criteria were known coronary artery disease, known chronic obstructive pulmonary disease, and not being able to perform physical treadmill testing and exercise. Patients were examined by a physician at inclusion to the study and the exclusion criterions were confirmed by medical records.

Assessments

An individualized protocol was applied to measure VO_{2peak} and peak heart rate (HR_{peak}), using the Cortex Metamax II portable metabolic test system (Cortex Biophysik GmbH, Leipzig, Germany) and the Polar S610i heart rate monitor (Polar Electro, Finland), respectively. The protocol has previously been described in patients with schizophrenia as well as in healthy individuals [14,16].

The patients were carefully familiarized with the test procedures and the treadmill when entering the laboratory. Warm-up was ten minute walking or running on the treadmill at an intensity corresponding to 60-70% HR_{peak}. The test started from warm-up speed (with minimum 5% inclination) after which the speed or the inclination was increased every minute (0.5-1 $km \cdot h^{-1}$ and 1-2%, respectively) to a level that brought the patient to exhaustion. The highest oxygen uptake and heart rate (HR) recorded during the last minute of the test were determined as VO_{2peak} and HR_{peak}, respectively. VO_{2peak} where also presented as $ml \cdot kg^{-0.75} \cdot min^{-1}$ to normalise for the differences in bodyweight between the patients [17].

We compared the patients VO_{2peak} with age and sex specific strata from the Nord-Trøndelag Health Study (the HUNT Study) [10]. The HUNT study is an epidemiological study of the general population in the neighbouring county to the university hospital. The HUNT Fitness study tested VO_{2peak} in 4 631 healthy individuals (20 to 90 years) using mixing chamber gas-analyzer ergospirometry (Cortex MetaMax II, Cortex, Leipzig, Germany) and an individualised protocol that has close resemblance to the protocol used in the present study. 14.1% of the participants reported to be inactive, defined as no activity or exercising less than once per week. For each patient with schizophrenia, we estimated a normative VO_{2peak}, namely the mean value defined in the HUNT Fitness study strata for the corresponding sex and age. We titled the VO_{2peak} estimated from sex and age strata independent of physical activity level, as HUNT general. The VO_{2peak} from age and sex strata for healthy inactive men and women were titled HUNT inactive. The percent of HUNT general and HUNT inactive VO_{2peak} was calculated as: (achieved VO_{2peak} ÷ age predicted VO_{2peak}) · 100.

In the HUNT Fitness study men and women below 44.2 $ml \cdot kg^{-1} \cdot min^{-1}$ and 35.1 $ml \cdot kg^{-1} \cdot min^{-1}$, respectively, were associated with higher cardiovascular risk factor profile [10]. The same VO_{2peak} values were used as threshold values when evaluating conventional CVD risk factors.

Morning fasting blood levels were taken. Serum glucose was analysed using Reflotron Plus system (Roche Diagnostics, Mannheim, Germany). HDL (high-density-lipoprotein) cholesterol, total cholesterol and triglyceride concentrations in serum were measured using a Modular P chemistry analyzer (Roche Diagnostics, Mannheim, Germany). LDL cholesterol was calculated using the Friedewald equation [18]. BP (blood pressure) was measured using a Maxi-Stabil 3 (Welch Allyn, Jungingen, Germany). Patients were sitting and had rested for at least 5 minutes. Risk factors were classified as follows: hypertension, diastolic pressure ≥ 90 mmHg and/or

systolic pressure ≥ 140 mmHg; elevated blood glucose, > 6.0 $mmol \cdot L^{-1}$; elevated total cholesterol, > 6.1 $mmol \cdot L^{-1}$ in patients < 30 years old, > 6.9 $mmol \cdot L^{-1}$ in patients 30-49 years old and > 7.8 $mmol \cdot L^{-1}$ in patients ≥ 50 years old; elevated LDL-cholesterol, 4.3 > $mmol \cdot L^{-1}$ in patients < 30 years old, 4.7 > $mmol \cdot L^{-1}$ in patients 30-49 years old and > 5.3 $mmol \cdot L^{-1}$ in patients ≥ 50 years old; reduced HDL-cholesterol, < 1.0 $mmol \cdot L^{-1}$; elevated triglyceride, > 2.6 $mmol \cdot L^{-1}$; obesity, BMI ≥ 30.0 $kg \cdot m^{-1}$ [19,20].

The short form (SF-36) was used to assess the physical health and mental health aspects of health related quality of life [21]. SF-36 consists of eight sub scores and can also be divided into a physical component score (PCS) and mental component score (MCS). 0 reflect the poorest health whereas 100 reflect the best health.

The Positive and Negative Syndrome Scale (PANSS) was used to evaluate the severity of symptoms of schizophrenia [22]. PANSS constitutes three scales measuring positive (productive symptoms), negative symptoms (deficit features) and general severity of illness. A total of 30 items are evaluated on a likert scale ranging from 1 (absent) to 7 (extreme) and added up to a total score as well as the three sub scores. In this study we used the positive and negative sub scores (7 items each) as well as the total score (30 items).

Analyses

We used the independent samples T-test to compare differences between men and women, between patients below and above the VO_{2peak} thresholds as well as between measured VO_{2peak} and HUNT general and HUNT inactive VO_{2peak}. We used the Pearson chi-square test to detect whether there was a significant association between patients above/below the VO_{2peak} threshold and prevalence of risk factors. We calculated the odds ratio for having one or more risk factors in the patients below threshold. The analysis was adjusted for age and sex. In multiadjusted analysis we also adjusted for the potential cofounding effect of smoking.

We used Pearson r to analyse correlations between VO_{2peak} ($ml \cdot kg^{-0.75} \cdot min^{-1}$) and each domain of the SF-36. The significance level (α) was set at $p < 0.05$ (2-tailed). Data are described as mean and standard deviation (SD), unless otherwise noted. SPSS statistical package, version 18.0 (SPSS Inc.), was applied to analyse results.

The study was approved by the regional committees for medical and health research ethics, middle Norway and conducted according to the Helsinki declaration. Written informed consent was obtained from all the included patients after the procedures were fully explained.

Results

Demographics

Age was 33.7 ± 10.4 years and 35.9 ± 11.5 years in men and women, respectively. The total PANSS, total positive PANSS and total negative PANSS score was 65 ± 17, 15 ± 6 and 17 ± 8 in men, and 68 ± 23, 16 ± 6 and 18 ± 8 in women, respectively.

Peak oxygen uptake

The VO_{2peak} for the men and women with schizophrenia are presented in Table 1. Individual VO_{2peak} values are plotted against age as well as normative VO_{2peak} strata from the HUNT Fitness study in Figure 1. VO_{2peak} in the men with schizophrenia was 84 ± 21% of age predicted HUNT inactive ($p < 0.001$) and 74 ± 19% of HUNT general ($p < 0.001$). The VO_{2peak} in the women with schizophrenia was not different from HUNT inactive (101 ± 28%) and HUNT general (89 ± 25%; n.s.). Age predicted VO_{2peak} was 44.5 ± 2.9 in HUNT inactive men, 50.3 ± 4.1 $ml \cdot kg^{-1} \cdot min^{-1}$ in HUNT general men, 35.2 ± 1.8 in HUNT inactive women and 40.0 ± 3.2 $ml \cdot kg^{-1} \cdot min^{-1}$ in HUNT general women.

Conventional risk factors

Risk factor assessment was lost in one male patient. Risk factors were present in 24 of 32 patients and of these five were above and 19 were below the thresholds. Among the eight patients without risk factors, six were above and two were below the thresholds ($\chi^2 = 7.6$, df = 1, $p = 0.006$). Based on the odds ratio adjusted for age and sex patients were 24.2 (95% CI = 1.5-505.6) times more likely to have one or more risk factors if they were below the VO_{2peak} threshold. When we also adjusted for smoking the odds ratio was 28.3 (95% CI = 1.6-505.6). Among the patients below the VO_{2peak} thresholds 10 patients had hypertension, 11 elevated glucose, 12 reduced HDL-cholesterol, 11 elevated triglyceride and 14 had obesity. Above the thresholds 2 patients had hypertension, 2 elevated glucose and 1 was obese. There were 8 smokers above the thresholds and 16 below. Differences in mean levels are presented in Table 2.

Quality of life

Results from the SF-36 questionnaire and correlations between SF-36 variables and VO_{2peak} are presented in Table 3.

Discussion

Peak oxygen uptake

The present results highlight reduced VO_{2peak} as a major risk factor for CVD in patients suffering from schizophrenia. The VO_{2peak} was 37.1 ± 9.2 and 35.6 ± 10.7 $ml \cdot kg^{-1} \cdot min^{-1}$ in men and women, respectively.

Table 1 Individual characteristics from the peak oxygen uptake test

Patient	Age	BW	VO_{2peak}	VO_{2peak}	VO_{2peak}	V_E	RER	HR
nr	years	Kg	$L \cdot min^{-1}$	$ml \cdot kg^{-1} \cdot min^{-1}$	$ml \cdot kg^{-0.75} \cdot min^{-1}$	$L \cdot min^{-1}$		Beats $\cdot min^{-1}$
Men								
1	21	76.5	3.64	47.6	140.7	126.1	1.07	186
2	21	95.3	3.72	39.1	122.0	107.7	1.09	175
3	24	66.6	3.65	54.9	156.6	138.1	1.19	211
4	25	159.5	4.25	26.6	94.7	134.0	1.19	154
5	25	120.9	3.21	26.5	88.0	115.8	1.09	160
6	26	65.0	3.15	48.5	137.6	100.4	1.22	185
7	26	107.9	4.07	37.7	121.6	126.3	1.23	177
8	27	96.7	3.50	36.1	113.5	102.4	1.11	186
9	27	107.2	3.36	31.3	100.9	94.7	1.04	180
10	28	100.6	2.96	29.4	93.2	69.2	1.00	190
11	29	66.7	2.99	44.8	128.1	121.7	1.13	183
12	31	78.0	3.76	48.2	143.3	118.6	1.41	188
13	31	70.1	3.14	44.8	129.6	106.9	1.10	165
14	37	114.0	3.87	34.0	110.9	109.2	1.10	153
15	40	98.7	2.38	24.1	76.0	65.2	1.00	143
16	41	77.4	3.29	42.0	126.1	110.4	1.21	153
17	41	89.5	3.80	42.5	130.6	105.7	1.22	164
18	41	117.1	3.88	33.1	109.0	118.6	1.06	165
19	45	122.3	3.38	27.7	91.9	125.4	1.08	150
20	47	122.7	2.94	24.0	79.7	89.2	1.00	153
21	50	75.7	3.46	45.7	134.8	90.8	1.08	156
22	58	109.6	3.07	28.1	90.6	91.2	1.07	160
Mean ± SD	33.7 ± 10.4	97.2 ± 24.0	3.43 ± 0.44	37.1 ± 9.2	114.5 ± 22.6	107.6 ± 19.0	1.12 ± 0.10	170 ± 17
Women								
1	22	61.7	2.98	48.3	135.4	94.1	1.18	180
2	24	53.3	2.28	42.8	115.6	54.0	0.99	173
3	28	66.4	2.82	42.6	121.2	97.1	1.14	169
4	28	73.5	2.33	31.7	92.8	66.4	1.20	176
5	28	80.3	2.44	30.4	91.0	93.0	1.20	188
6	34	51.6	2.61	50.7	135.6	79.8	1.27	194
7	41	144.5	2.46	17.0	59.0	71.0	1.02	150
8	42	75.5	3.30	43.7	128.8	108.0	1.20	163
9	44	64.9	1.98	30.5	86.6	56.0	1.16	175
10	48	55.5	1.70	30.7	83.6	73.2	1.10	168
11	58	91.8	2.12	23.1	71.5	74.1	1.13	151
Mean ± SD	35.9 ± 11.5	74.5 ± 26.3	2.46 ± 0.46	35.6 ± 10.7	101.9 ± 26.6	78.8 ± 17.4	1.15 ± 0.08	172 ± 14

BW, body weight; VO_{2peak}, peak oxygen uptake; HR, heart rate; V_E, total pulmonary ventilation; RER, respiratory exchange ratio; SD, standard deviation

These values are considerable higher than previous assumptions [3,13]. Strassnig et al. [3] reported VO_2 values of 18.7 ± 6.8 and 13.4 ± 4.6 $ml \cdot kg^{-1} \cdot min^{-1}$in the men and women, respectively (mean age of 45.1 ± 10.1 years). These low VO_{2peak} values is to some degree explained by the high body weight (mean BMI of 36.7 ± 7.5 $m \cdot kg^2$). However, there are some indications of an underrating of these patients' VO_{2peak}. First, the patients only reached a low peak heart rate (142 ± 21 $beats \cdot min^{-1}$). Secondly, both Carlsson et al. [13] and Strassnig et al. [3] applied a cycle ergometer test which is known to depend more on the patients motivation than a treadmill test. Patients with schizophrenia terminate cycle tests already at submaximal work loads, in contrast to health subjects [23]. Thirdly, subjects tested on a cycle ergometer achieve 7-16% lower VO_{2max} compared with a maximal treadmill test, even when HR_{peak} is not significantly different [24,25].

In contrast to Strassnig et al. [3], the present results demonstrate that the mean VO_{2peak} in the women was similar to the men with schizophrenia, even though the age was similar (36 years in women versus 34 years in

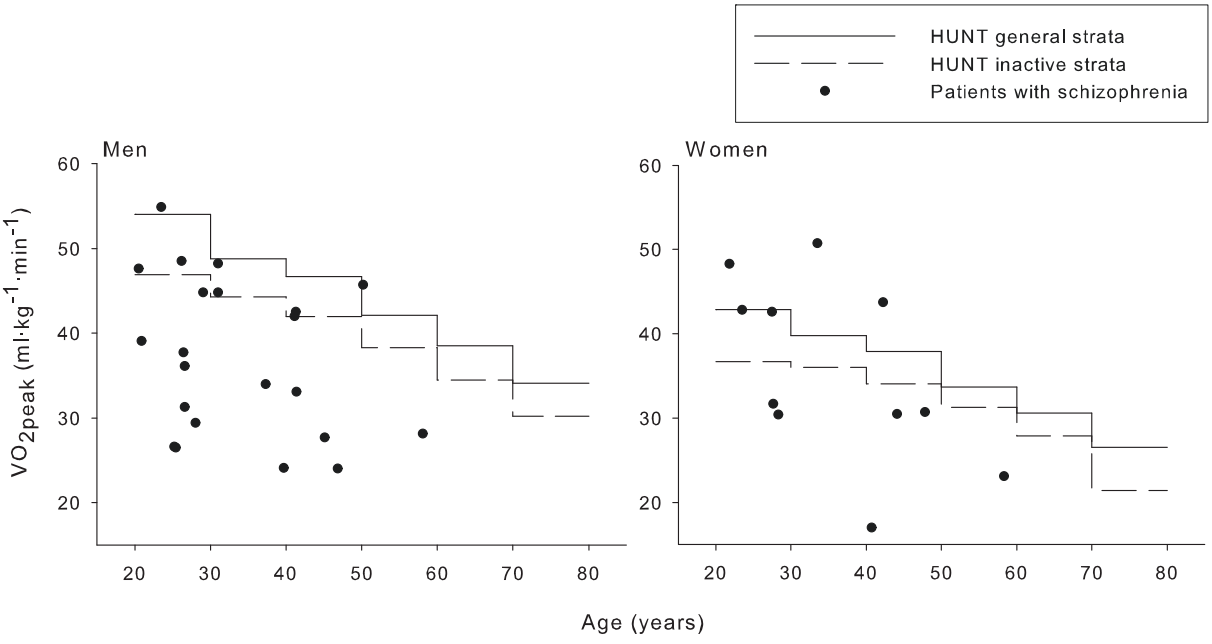

Figure 1 Peak oxygen uptake in patients with schizophrenia and normative healthy men and women. Normative strata are adopted from the HUNT fitness study [10]. HUNT general strata are age and sex specific strata regardless of physical activity level.

men). Women normally have about 10 ml·kg^{-1}·min^{-1} lower VO_{2peak} compared to men at the same age [10]. The mean body weight was 97.2 and 74.5 kg in men and women, respectively, which partially explain the difference in VO_{2peak}.

Comparison with healthy individuals

The comparison with normalised VO_{2peak} from the HUNT Fitness study, confirm our hypothesis that VO_{2peak} is reduced in men with schizophrenia. The VO_{2peak} in the women with schizophrenia was almost identical (101%) to inactive healthy HUNT women. Even lower VO_{2peak} in men with schizophrenia compared to normative inactive men might suggest that more than just inactivity contribute the reduced VO_{2peak}. The VO_{2peak} in the men with schizophrenia is similar to normative healthy men aged 60-69 years [10]. In other words, the VO_{2peak} in the men with schizophrenia is comparable to healthy men that are about 30 years older. Patients with schizophrenia actually have 15-25 years shorter life expectancy than the general population [26,27]. It is noteworthy that the VO_{2peak} presented in the HUNT Fitness study is somewhat higher than previous described populations with regard to objectively measured VO_{2peak} [28-31].

Cardiovascular risk

People with reduced VO_{2peak} are consistently being associated with increased risk of cardiovascular and all-cause mortality. Kodama et al. [5] found that 3.5 ml·kg^{-1}·min^{-1} (1 MET) increases were associated with 13% and 15% reductions in all-cause mortality and CVD/coronary heart disease, respectively. Aspenes et al. [10] found that 5 ml·kg^{-1}·min^{-1} lower VO_{2peak} correspond to 56% higher odds of having a cluster of cardiovascular risk factors.

The comparison of patients with schizophrenia below and above the VO_{2peak} thresholds suggested by Aspenes et al. [10] confirm that patients below these thresholds have higher prevalence of risk factors compared with patients above the thresholds. Based on the odds ratio patients were 28.3 times more likely to have one or more risk factors if they were below the VO_{2peak} thresholds. When comparing mean levels above and below thresholds, all risk factors, except glucose, was better in the patients above the thresholds. These findings suggest a strong connection between the patients VO_{2peak} and the conventional risk factors for CVD, as confirmed in other populations [10,32].

Our data are not quite consistent with findings from US suggesting that especially women with schizophrenia are at high risk of developing metabolic syndrome [33].

Table 2 Characteristics[a] in patients below and above the threshold peak oxygen uptake (VO_{2peak})[b]

		Men	
	VO_{2peak} (< 44.2) (n = 15)	**VO_{2peak} (≥ 44.2) (n = 6)**	**Mean difference (95% CI)**
Systolic pressure (mm Hg)	139.4 ± 16.8	125.7 ± 11.0	-13.8 (-29.6 to 2.0)
Diastolic pressure (mm Hg)	87.4 ± 7.0	84.3 ± 5.0	-3.0 (-9.7 to 3.6)
Total cholesterol ($mmol \cdot L^{-1}$)	5.2 ± 0.7	4.5 ± 0.5	-0.7 (-1.3 to -0.0)
HDL cholesterol ($mmol \cdot L^{-1}$)	1.0 ± 0.3	1.6 ± 0.4	0.5 (0.2 to 0.9)
LDL cholesterol ($mmol \cdot L^{-1}$)	3.2 ± 0.6	2.5 ± 0.6	-0.7 (-1.3 to -0.1)
Triglyceride ($mmol \cdot L^{-1}$)	2.1 ± 1.1	0.9 ± 0.2	-1.2 (-1.8 to -0.6)
Glucose ($mmol \cdot L^{-1}$)	6.4 ± 2.0	5.8 ± 0.6	-0.6 (-2.4 to 1.1)
BMI ($kg \cdot m^{-2}$)	33.0 ± 5.5	23.6 ± 2.4	-9.5 (-14.5 to -4.5)
		Women	
	VO_{2peak} (<35.1) (n=6)	**VO_{2peak} (≥35.1) (n=5)**	
Systolic pressure (mm Hg)	121.6 ± 7.9	103.8 ± 11.9	-17.8 (-32.6 to -3.0)
Diastolic pressure (mm Hg)	80.8 ± 4.4	68.8 ± 8.8	-12 (-22.1 to -1.9)
Total cholesterol ($mmol \cdot L^{-1}$)	5.0 ± 0.7	4.6 ± 1.0	-0.4 (-1.5 to 0.8)
HDL cholesterol ($mmol \cdot L^{-1}$)	1.3 ± 0.3	1.8 ± 0.3	0.5 (0.1 to 0.9)
LDL cholesterol ($mmol \cdot L^{-1}$)	2.9 ± 0.9	2.5 ± 1.1	-0.4 (-1.8 to 1.0)
Triglyceride ($mmol \cdot L^{-1}$)	1.8 ± 0.7	0.8 ± 0.3	-1.0 (-1.7 to -0.3)
Glucose ($mmol \cdot L^{-1}$)	6.1 ± 1.5	4.8 ± 0.4	-1.3 (-2.9 to 0.2)
BMI ($kg \cdot m^{-2}$)	31.2 ± 10.9	23.6 ± 4.5	-7.5 (-19.5 to 4.4)
		All	
	< threshold (n = 21)	≥ threshold (n = 11)	
Systolic pressure (mm Hg)	134.7 ± 16.8	115.7 ± 15.7	-19.0 (-31.8 to -6.3)
Diastolic pressure (mm Hg)	85.63 ± 6.9	77.3 ± 10.4	-8.4 (-14.9 to -1.9)
Total cholesterol ($mmol \cdot L^{-1}$)	5.1 ± 0.7	4.6 ± 0.7	-0.6 (-1.1 to -0.0)
HDL cholesterol ($mmol \cdot L^{-1}$)	1.1 ± 0.3	1.6 ± 0.3	0.5 (0.0 to 0.1)
LDL cholesterol ($mmol \cdot L^{-1}$)	3.1 ± 0.7	2.5 ± 0.8	-0.6 (-1.2 to -0.1)
Triglyceride ($mmol \cdot L^{-1}$)	2.0 ± 1.0	0.9 ± 0.3	-1.1 (-1.6 to -0.7)
Glucose ($mmol \cdot L^{-1}$)	6.3 ± 1.8	5.3 ± 0.7	-1.0 (-2.2 to 0.2)
BMI ($kg \cdot m^{-2}$)	32.4 ± 7.5	23.6 ± 3.3	-8.8 (-13.7 to -3.9)

[a]mean ± SD.

[b]44.2 $ml \cdot kg^{-1} \cdot min^{-1}$ in men and 35.1 in women based on the results from Aspenes et al. [10].

HDL, high-density lipoprotein; LDL, low-density lipoprotein; BMI, body mass index.

Table 3 SF-36 items scores[a] and Pearson correlation coefficient between SF-36 items and peak oxygen uptake[b]

	Women (N = 11)		**Men (N = 19)**		**All (N = 30)**	
SF-36 items	**Mean ± SD**	***r***	**Mean ± SD**	***r***	**Mean ± SD**	***r***
Physical function (PF)	76.4 ± 28.1	0.68*	82.6 ± 20.2	0.48*	80.3 ± 23.1	0.58***
Role physical (RP)	56.8 ± 35.5	0.61*	67.1 ± 30.1	0.10	63.3 ± 32.0	0.34
Bodily pain (BP)	77.5 ± 24.7	0.06	73.8 ± 26.1	0.11	75.2 ± 25.2	0.26
General health (GH)	58.1 ± 17.6	0.72*	63.6 ± 19.9	0.42	61.6 ± 19.0	0.53**
Vitality (VT)	52.7 ± 22.8	0.71*	51.8 ± 18.6	0.30	52.2 ± 19.9	0.47*
Social function (SF)	51.1 ± 29.8†	0.41	74.3 ± 17.4	0.34	65.8 ± 25.9	0.41*
Role emotional (RE)	42.4 ± 33.7†	0.39	73.7 ± 37.8	0.25	62.2 ± 38.9	0.35
Mental health (MH)	55.3 ± 15.1	0.68*	67.0 ± 16.5	0.08	62.7 ± 16.7	0.34
Physical component (PCS)	49.1 ± 10.3	0.72*	48.2 ± 7.6	0.37	48.6 ± 8.6	0.51**
Mental component (MCS)	36.5 ± 8.4†	0.52	45.6 ± 10.2	0.16	42.2 ± 10.4	0.34

[a]Patients with schizophrenia

[b]$ml \cdot kg^{-0.75} \cdot min^{-1}$.

* $p < 0.05$, **$p < 0.005$, *** $p < 0.001$ Pearsons r. † $p < 0.05$ compared to men, independent T-test.

This is most likely caused by the women's fitness level in the present study, as VO_{2peak} have been described as a strong independent predictor of metabolic syndrome [32].

These results emphasize that evaluation of VO_{2peak} should be incorporated into routine clinical practice for risk prediction. The prognostic value of VO_{2peak} is beyond that predicted from other conventional risk factors [6,34]. Even in individuals with present risk factors, the higher levels of VO_{2peak} seem to confer a significant protective effect [4]. Reduced VO_{2peak} is a modifiable risk factor, and eight weeks aerobic high intensity interval training has provided significant improvements of VO_{2peak} both in healthy populations [16] and in patients with schizophrenia [14]. Furthermore, to reduce the risk of CVD, the interventions are probably more dependent on improving VO_{2peak} than increasing physical activity level alone [35,36].

Quality of life

Our findings of lower SF-36 social function, role emotion and mental component score among women than among men might reflect a sex difference in the general population. Lower scores for women than for men have been identified in normative adults [37]. The gender-specific correlations between items of SF-36 and VO_{2peak} suggest major gender differences in self-perception. Only the correlation with between SF-36 physical functioning and VO_{2peak} was significant in men, whereas six correlations with the SF-36 were significant in women. In all subjects together the VO_{2peak} correlated with the patient's perception of physical function, general health, vitality, social function, and physical component score. With some exceptions, these findings are consistent with correlations between SF-36 variables and BMI in patients with schizophrenia [38]. In line with Strassnig et al. [38] we found a significant correlation with the physical component score but not the mental component score, suggesting that reduced VO_{2peak} mainly is perceived as a physical health problem, not mental. Contrary, both the mental and physical health components of QOL are found related to estimated VO_{2peak} in healthy men [12]. An interesting note is, however, that the patients with lower VO_{2peak} seemed to experience lower vitality and social functioning. Sedentary people are associated with greater risk of low vitality [39]. QOL are found to improve in a dose dependent manner in sedentary women when increasing physical activity level [40].

Limitations

There are some limitations of the study. First, the sample size is low. Secondly, the patients were included in the study based on request to take part in exercise intervention studies. However, all eligible patients at the department were asked to participate in these studies. Thirdly, severe ill patients with schizophrenia, with poor insight to their illness, might have difficulties to evaluate their perception of QOL.

Conclusions

Men with schizophrenia have lower VO_{2peak} than men in the general population. Patients with a VO_{2peak} below 44.2 $ml \cdot kg^{-1} \cdot min^{-1}$ (men) and 35.1 $ml \cdot kg^{-1} \cdot min^{-1}$ (women) have higher odds of having one or more risk factors for cardiovascular disease. Low VO_{2peak} compromise patients' perceived physical health. VO_{2peak} should be regarded as least as important as the conventional risk factors for CVD and evaluation of VO_{2peak} should be incorporated in clinical practice. Finally, these finding represent an urging need for developing effective physical training interventions for patients with schizophrenia.

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Author details

[1]Norwegian University of Science and Technology, Faculty of Medicine, Department of Neuroscience, Trondheim, Norway. [2]St. Olavs University Hospital, Division of Psychiatry, Department of Research and Development (AFFU), Trondheim, Norway. [3]St. Olavs University Hospital, Division of Psychiatry, Department of Østmarka, Trondheim, Norway. [4]Norwegian University of Science and Technology, Faculty of Medicine, Department of Circulation and Medical Imaging, Trondheim, Norway. [5]St.Olavs University Hospital, Department of Physical Medicine and Rehabilitation, Trondheim, Norway. [6]Hokksund Medical Rehabilitation Centre, Hokksund, Norway. [7]Telemark University College, Department of Sports and Outdoor Life Studies, Bø, Norway.

Authors' contributions

GM, JH, JH and JH designed the study. JH and GEN recruited patients, performed VO_{2peak} testing and other data acquisition. GM and JH undertook the statistical analysis and JH wrote the first draft of the paper. All authors have contributed to and have approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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