Master's thesis

NTNU
Norwegian University of Science and Technology
Faculty of Medicine and Health Sciences
Department of Circulation and Medical Imaging

Daniel Leven Gjerdset

Cardiorespiratory reference data in Norwegian post myocardial infarction patients: A Cross-sectional study

A sub-study of The Norwegian Trial of Physical Exercise After Myocardial Infarction (NorEx)

Master's thesis in Physical Activity and Health (Exercise Physiology)
Supervisor: Ulrik Wisløff
Co-supervisor: Arnt Erik Tjønna
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Infographic of my study

Cardiorespiratory reference data in Norwegian post myocardial infarction patients: A Cross-sectional study

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Exercise physiology student doing a sub-study of the world's longest and largest training study

Did you know?

7 million
experience myocardial infarction each year.

Cardiorespiratory fitness (CRF)
measured as peak oxygen uptake ($VO_{2\,peak}$): Most important single predictor of both cardiac and all-cause death.

American Heart Association:
"CRF should be regarded as a vital sign along with established risk factors".

Aim: Provide baseline values for $VO_{2\,peak}$ and cardiovascular physiology data on post MI patients using cardiopulmonary exercise test (CPET).

Patients

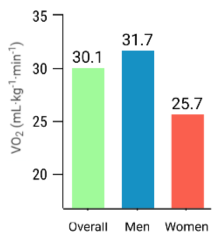
70 patients measured their CRF (69= treadmill, 1= cycle ergometer)

Age range 33-78 yr

	Men n=52	Women =18
Age (years)	65.0 ± 8.5	63.7 ± 9.3
Height (cm)	179.2 ± 5.7	165.9 ± 5.2
Body mass (kg)	90.5 ± 12.4	75.8 ± 14.5
BMI (kg · min-2)	28.2 ± 3.6	27.6 ± 5.4
Never smoked (%)	36.5	27.8
Smoked daily before (%)	44.2	44.4
Current smoker (%)	5.8	11.1

Monitored with electrocardiogram, and blood pressure was measured before and after test.

What did we find?



Physiological characteristics

Woman, age: 66 yr
23.2 ($mL \cdot kg^{-1} \cdot min^{-1}$)

	Men	Women
Peak heart rate ($beat \cdot min^{-1}$)	158 ± 17	156 ± 20
Heart rate recovery, 1 min ($beat \cdot min^{-1}$)	28.4 ± 13.2	26.5 ± 8.5
Peak oxygen pulse ($beat \cdot min^{-1}$)	18.0 ± 3.9	12.5 ± 2.9
Pre exercise postural BP (mmHg)	151/92	157/92
Post exercise postural BP (mmHg)	176/105	186/106
BORG	19 ± 1	19 ± 1

Heart rate recovery 1 minute after peak heart rate, reflects reactivation of the parasympathetic nervous system, Peak oxygen pulse: oxygen uptake per heartbeat, an indirect reflection of left ventricular stroke volume, BP: blood pressure, systolic/diastolic, BORG: subjective perception of fatigue at VO_{2peak} (6-20).

9/70
patients had higher $VO_{2\,peak}$ compared to healthy individuals at their age and sex from Trøndelag Health Study (HUNT).

Physical activity data

Patients answered a self-administered questionaire about leisure time physical activity (average pr week). Overall n=64.

2-3
times pr week

Heavy breath and sweat

30-60
min

were the most frequent answers among our post MI patients.

After 3.5 yr, the reference material may:

1. *Lead to a more accurate assessment of the impact of CRF on health outcomes.*
2. *Improve diagnostics.*
3. *Be an important tool for prescription of cardiac rehabilitation and for health professionals examining patient's health risks in the future.*
4. *Encourage people to improve their CRF and be more physically active.*

CERG Our heart is in the future

For further details about the results, you are welcome to read my scientific article below or visit **ntnu.no/cerg/norex** for more information about NorEx.

NorEx

Abstract

Purpose: To establish a reference material of objectively measured peak oxygen uptake, (VO_{2peak}) and cardiovascular physiology data on Norwegian post myocardial infarction (MI) patients.

Methods: Maximal and submaximal levels of oxygen uptake (VO_2), heart rate, oxygen pulse, and rating of perceived exertion (Borg scale: 6-20) was measured in 52 men (65.0 ± 8.5 yr, 179.2 ± 5.7 cm, 90.5 ± 12.4 kg) and 18 women (63.7 ± 9.3 yr, 165.9 ± 5.2 cm, 75.8 ± 14.5 kg) during treadmill or cycle ergometry.

Results: When dividing the population into age groups $\leq$65 yr and >65 yr, we observed the highest VO_{2peak} in men and women in the youngest age group (34.8 ± 8.0 $mL \cdot kg \cdot min^{-1}$ vs. 27.5 ± 5.6 $mL \cdot kg^{-1} \cdot min^{-1}$, sex differences $p<0.16$). We did not observe any significant difference in peak heart rate between age groups or sexes. The highest oxygen pulses, a reflection of left ventricular stroke volume, was observed among the youngest men (20.3 ± 3.8 $mL \cdot beat^{-1}$) compared to older men (15.9 ± 2.6 $mL \cdot beat^{-1}$) ($p<0.001$). Similar observations were made for the younger women (13.6 ± 1.8 $mL \cdot beat^{-1}$) compared to the older women (11.4 ± 3.4 $mL \cdot beat^{-1}$) ($p=0.119$). The highest heart rate recovery (HR recovery) 1 minute after peak heart rate was observed among both men (29.8 ± 12.0 $beat \cdot min^{-1}$) and women <65 yr (26.7 ± 7.0 $beat \cdot min^{-1}$) with no significant difference between sexes. Borg scores underestimated the relative exercise intensity at lower intensities in both sexes, but had fairly good accuracy at higher intensities.

Conclusion: This is the start of a reference material on objectively measured cardiorespiratory fitness (CRF) and cardiovascular physiology data in post MI patients. The data may contribute to improve diagnostics, be an important tool for prescription of cardiac rehabilitation and for health professionals examining patient's health risks in the future.

Sammendrag

Hensikt: Å lage et referansemateriale av direkte målt peak oksygen opptak (VO_{2peak}) og kardiovaskulære data på norske pasienter som har gjennomgått et hjerteinfarkt (MI).

Metode: Maksimale og submaksimale nivåer av oksygen opptak (VO_2), hjertefrekvens, oksygenpuls og opplevd grad av anstrengelse (Borg-skala: 6-20) ble målt hos 52 menn (65.0 ± 8.5 år, 179.2 ± 5.7 cm, 90.5 ± 12.4 kg) og 18 kvinner (63.7 ± 9.3 år, 165.9 ± 5.2 cm, 75.8 ± 14.5 kg) på tredemølle eller ergometer sykkel.

Resultater: Ved å dele pasientene inn i aldersgrupper $\leq$65 år og >65 år, observerte vi høyeste VO_{2peak} hos menn og kvinner i den yngste aldersgruppen (34.8 ± 8.0 mL·kg·min^{-1} vs. 27.5 ± 5.6 mL·kg^{-1}·min^{-1}, kjønnsforskjeller $p<0.16$). Vi observerte ingen vesentlig forskjell i peak hjertefrekvens mellom aldersgrupper eller kjønn. Høyeste oksygenpuls (en indikator på slagvolum i venstre ventrikkel) ble observert blant de yngste mennene (20.3 ± 3.8 mL·slag^{-1}), sammenlignet med eldre menn (15.9 ± 2.6 mL·slag^{-1}) ($p<0.001$). Lignende resultater ble også observert blant de yngste kvinnene (13.6 ± 1.8 mL·slag^{-1}) sammenlignet med den eldre aldersgruppen (11.4 ± 3.4 mL·slag^{-1}) ($p=0.119$). Høyeste hjertefrekvensnedgang (HR recovery) 1 minutt etter peak hjertefrekvens, ble observert blant både menn (29.8 ± 12.0 slag·min^{-1}) og kvinner <65 år (26.7 ± 7.0 slag·min^{-1}) med ingen vesentlig forskjell mellom kjønn. Borg-skala undervurderte den relative treningsintensiteten ved lavere intensitet hos begge kjønn, med ganske god estimering ved høyere intensitet.

Konklusjon: Dette er starten på et referansemateriale på objektivt målt kardiorespiratorisk kondisjon (CRF) og kardiovaskulære data blant pasienter med tidligere MI. Dataene kan bidra til å forbedre diagnostikken, være et viktig verktøy for hjerterehabilitering og for helsepersonell som undersøker pasientens helserisiko i fremtiden.

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Selected abbreviations

ACSM	American College of Sports Medicine
AHA	American Heart Association
CPET	Cardiopulmonary Exercise Test
CR	Cardiac rehabilitation
CRF	Cardiorespiratory fitness
CVD	Cardiovascular disease
ECG	Electrocardiogram
HR	Heart rate
HR_{peak}	Peak heart rate
HR recovery	Heart rate recovery
HUNT	The Trøndelag Health Study
MET	Metabolic equivalent
MI	Myocardial infarction
MoCA	The Montreal Cognitive Assessment
O_{2pulse}	Oxygen pulse
PAI	Physical Activity Index
RER	Respiratory exchange ratio
VO_2	Oxygen uptake
VO_{2max}	Maximal oxygen uptake
VO_{2peak}	Peak oxygen uptake

Introduction

Myocardial Infarction (MI) is an increasing health problem worldwide, and contributes to one of the greatest medical and scientific challenges in our generation (1). Over the last three decades, a significant amount of literature has demonstrated that the most important single predictor of both cardiac and all-cause death is peak oxygen uptake (VO_{2peak}) (2–6). Despite this, VO_{2peak} as a measure of cardiorespiratory fitness (CRF) has received limited attention from the medical community and health professionals, and has a tendency to be overlooked due to general uncertainty about its therapeutic implications (2,7). In addition, there is no valid reference material on VO_{2peak} and cardiovascular physiology data in post MI patients measured objectively with a cardiopulmonary exercise test (CPET). The consensus between several studies show that reference material on CRF can be used to optimize the risk level and treatment, contribute to chronic disease prevention, and to provide a healthier and longer life span (2,8).

Myocardial infarction

Globally, over 7 million people experience MI each year (1). In Europe, MI is the leading cause of death with about 2 million annually (1). In addition, more than 20% suffer a second cardiovascular event within the first year (1). A commonly applied definition of MI is given by the European Society of Cardiology / American College of Cardiology Committee:

"… myocardial cell death due to prolonged ischemia, which is the result of perfusion imbalance between supply and demand" (9).

MI is estimated to cost the European Union economy €60 billion a year. According to the World Health Organization, if the population adhere to official guidelines for physical activity, 30 % of these deaths could be prevented (1). With a rapidly aging population, MI is the main cause of reduced life expectancy in Europe (1). Several contemporary studies have demonstrated that a higher CRF is associated with reduced risk of future cardiovascular diseases (CVD) and other adverse health outcomes in post MI patients (2–4).

Myocardial infarction and Cardiorespiratory fitness

CRF reflects the ability to take up, transport and utilize oxygen to perform physical work (2). Multiple studies have shown the strong inverse association between CRF and all-cause mortality (2,3,7,8), and the American Heart Association (AHA) has stated that it should be regarded as a vital sign, along with established risk factors such as smoking, high cholesterol, hypertension and type 2 diabetes mellitus (2). Some studies have even indicated that CRF is potentially a stronger predictor of mortality than factors repeatedly proven to predict mortality (2,3), and that CRF has a comparable impact on longevity as the most commonly prescribed cardioprotective medicine (7). Furthermore, the research also states that *"…there needs to be accelerated efforts to include CRF as a routine health measure"* (10). Maximal oxygen uptake (VO_{2max}) has been recognized as the gold standard for CRF (11). VO_{2max} is directly related to the integrated function of numerous systems such as cardiac, pulmonary, vasculature, and skeletal muscle, and thus considered a reflection of overall health status (2,11). VO_{2max} inevitably declines with age and is influenced by several factors such as body composition, exercise- and lifestyle habits (10).

Several studies have demonstrated the crucial importance of maintaining or improving CRF in post MI patients (2,12). In population based studies an increase of 1 $mL \cdot kg^{-1} \cdot min^{-1}$ has shown to be associated with 10-15% reduced risk of all-cause mortality, and that the largest health and mortality benefits occurs when progressing from least fit to more fit (2,4,6). In a paper by Franklin and colleagues, post MI patients that participated in cardiac rehabilitation (CR) improving their CRF by 1 metabolic equivalent (MET, i.e. 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$), had 8% to 14% reduction in mortality during a 19-year follow-up (7). Another study from Shaya et al. (12) revealed that 1-MET increase was associated with an 8-10% reduction in the risk of early MI subsequent after the first MI. This study also revealed that a higher CRF was associated with reduced mortality 28, 90, and 365 days after post MI event. De Schutter and colleagues (13) also found that exercise-based CR was associated with reduction in mortality and reinfarction post MI. Furthermore, two studies of Kavangah et al. (5,6) demonstrated that in both men and women, directly measured VO_{2peak} was a strong independent predictor of cardiac mortality.

Cardiopulmonary exercise test and Myocardial infarction

AHA stated that *"…the longer and more intensely a patient can exercise during an exercise test, the less likely he or she will die soon from coronary artery disease or other causes"* (11).

Patients can measure their CRF by estimation, which is often calculated by speed, time or incline of the treadmill or cycle ergometer and reported in METs. This method can be useful to access prognostic risk in patients entering CR or to establish baseline fitness (14,15). Unfortunately, estimation may lead to inaccurate interpretations and estimation errors of ± 3.4 to 4.4 $mL \cdot kg^{-1} \cdot min^{-1}$ has been reported (8). In addition, allowing patients to hold handrails while walking or running, may lead to a higher work rate and increase the estimation error of CRF (2). AHA has expressed that CPET will provide a more accurate measurement, and this method is actually recognized as the gold standard for measuring CRF (11). CPET gives a highly accurate (± 2%), reliable and comprehensive assessment of all systems involved in the response to aerobic exercise (11,16). Furthermore, it can give important information about underlying mechanisms for exercise intolerance, abnormal exertion symptoms and diagnosis (11).

For example, oxygen pulse (O_{2pulse}) which is the amount of oxygen ejected from the left ventricle per heartbeat, can be used to detect myocardial ischemia and atrial fibrillation (16). Usually, a flattening or downward displacement of O_{2pulse} during CPET would likely reflect a cardiogenic limitation to exercise (16). Another variable that reflects prognostic value is the heart rate recovery (HR recovery), which is defined as the decrease in heart rate (HR) from peak exercise to 1 minute after the cessation of exercise. This variable is shown to be a powerful predictor of overall mortality (17,18). After exercise, an immediate decrease in HR is considered to be a function of reactivation of the parasympathetic nervous system and abnormal values is reported to be <12 $beat \cdot min^{-1}$ from the HR at peak exercise (17,18).

A benefit of direct measurement compared to an estimation of CRF is the ability to identify patients effort, with tests often terminated when patients reach a plateau in VO_2, despite increased workload (19). Another advantage with direct measurement is the access to the respiratory exchange ratio (RER), which is defined as the ratio between carbon dioxide output and oxygen uptake (VO_2), obtained exclusively from ventilatory gas analysis. RER is found to be an accurate and reliable variable of the patients effort, and a value above >1.05 is often used as a secondary criteria for researching VO_{2max} (16). For post MI patients, different pathological conditions may affect and limit oxygen uptake at peak effort. For this reason, the term VO_{2peak} is more commonly used, where a plateau in VO_2 is not frequently observed, which is the main criteria to define whether the true VO_{2max} was achieved (2).

CPET has been demonstrated to be a safe method to access CRF, with a low risk of cardiac events (16). A study has reported that health practitioners should integrate CPET into evaluation of patient treatment in order to determine whether their prescription of exercise/medicine leads to clinically meaningful improvements in CRF (20). To optimize CPET in clinical settings and to facilitate interpretation, a reference material is necessary (21). A study measuring VO_{2peak} in healthy Norwegian men and women from age 20-90 yr, demonstrated that a 5 $mL \cdot kg^{-1} \cdot min^{-1}$ decrease in VO_{2peak} was associated with a 56% higher prevalence of cardiovascular risk factors in both sexes (22). Reference values in this population could therefore be useful in clinical decision-making, establishing prognostic values between peers and identifying patients with a higher risk of getting a cardiovascular event at present or in the future (21).

Both Rognmo et al. (23) and Moholdt et al. (24) performed CPET in Norwegian men and women with post MI aged 57-60 yr, with mean VO_{2peak} of 31.8 and 31.6 $mL \cdot kg^{-1} \cdot min^{-1}$, respectively. Another study, Keteyian et al. (25) measured a mean VO_{2peak} of 21.8 and 22.4 $mL \cdot kg^{-1} \cdot min^{-1}$ in American men and women with post MI, respectively. Previously, CPET was not used regularly due to costs associated with equipment and lack of trained professionals (2). The majority of studies in post MI patients are conducted in men and used cycle ergometry (3,5,7,13,15,26). This method can underestimate VO_{2peak} with 10-20% for patients not familiar with cycling (2). Currently, there exists no valid reference material for CRF and cardiovascular physiology data in post MI patients, performed on a treadmill and measured directly using CPET.

Aim

The aim of this thesis was to provide baseline values on VO_{2peak} and cardiovascular physiology data in Norwegian post MI patients that will end up as a reference material in the future.

Methods

NorEx

The Norwegian Trial of Physical Exercise after Myocardial Infarction (NorEx) is a nationwide registry-based, three-arm, multicenter randomized clinical trial for secondary prevention and rehabilitation of patients who have suffered MI. The aim is to determine the effects of 3.5 years of supervised physical exercise on mortality and cardiovascular morbidity. The total duration of the study is expected to be 15 years, with the intervention period for the whole study from 2021-2025 and long-term follow-up from 2025-2034. Men and women with MI during 2013-2022 registered in the Norwegian MI-registry receives an invitation to participate in the study. The invitation contains information about the study design, a consent form and a self-administered questionnaire about the patient's physical and mental health. The questionnaire response is used to determine eligibility for invitation to a screening at the local hospital. A flowchart of the estimated recruitment and randomization procedure is presented in Figure 1.

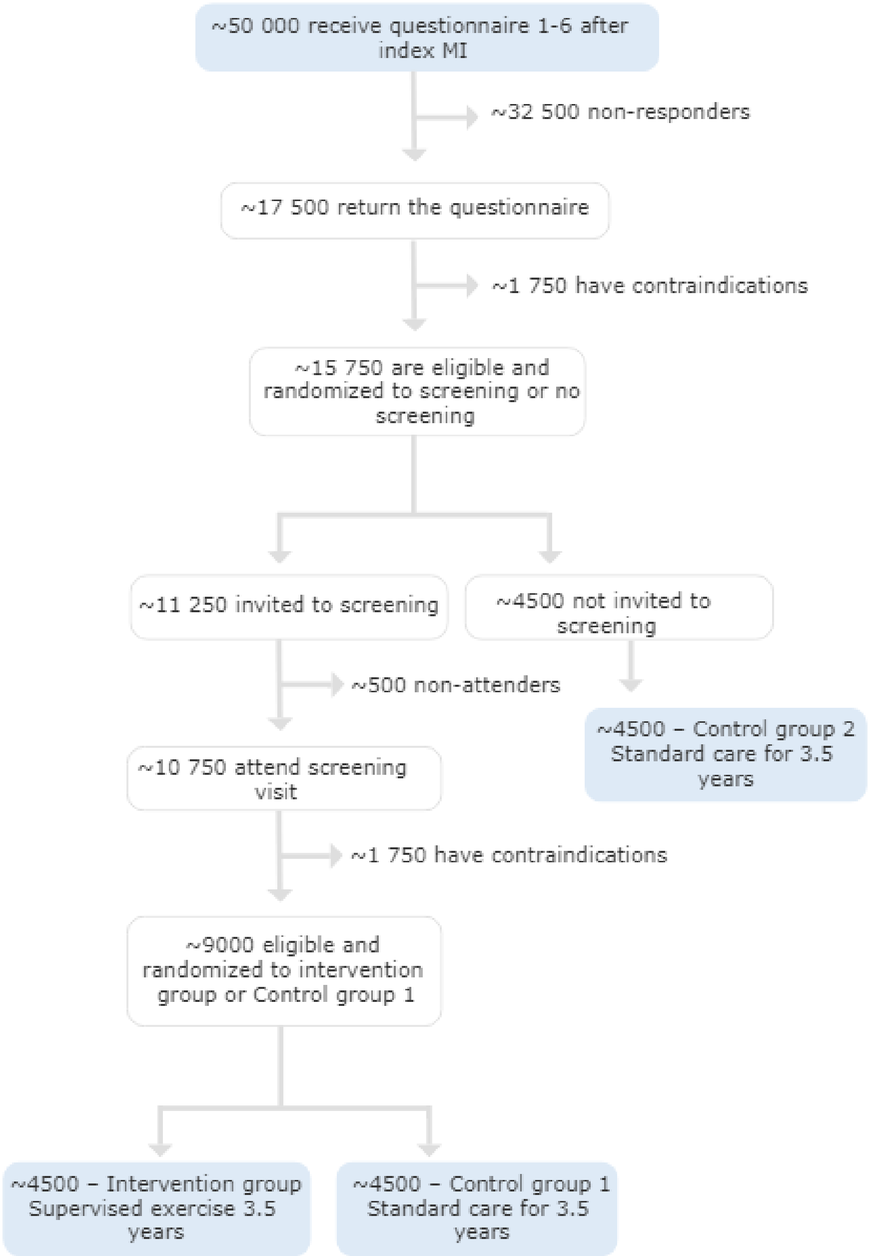

Figure 1. An estimated flowchart of the recruitment and randomization procedure in NorEx.

Establishing baseline material on CRF in post MI patients

NorEx-focus is a part of NorEx that draws a random sample of 300 MI patients for testing of cognitive function and CRF measured with CPET at baseline, 1- and 3.5-year follow-up, respectively. The testing occurred before the NorEx intervention with n=150 from the intervention group and n=150 from Control group 1. This cross-sectional sub-study of NorEx aims to establish baseline reference material on VO_{2peak} and cardiovascular physiology data using CPET in post MI patients, in Trondheim, Norway. The current baseline data was collected between November 2020 and March 2021. Inclusion and exclusion criteria are presented in Table 1.

Table 1. Inclusion and exclusion criteria in NorEx.

Inclusion criteria	Exclusion criteria
• Age >18 years • Can communicate in Norwegian or another Scandinavian language • Hospital admission due to type 1 acute myocardial in 2013-2022 • Signed consent form	• Regular physical activity level above the exercise intervention • Participating in endurance sport competitions • Diagnosed dementia • Known alcohol or drug abuse • Severe psychiatric disorder • Kidney failure leading to dialysis • Diagnosed heart disease contradicting moderate or high intensity physical activity • Uncontrolled hypertension (systolic /diastolic blood pressure > 210/ 110 mmHg) • Severe illness with reduced life expectancy or which prevents training with moderate or high intensity • Residing in a nursing home or other institution • Participate in another intervention study with physical activity / training as intervention

Initially, the following hospitals were responsible for testing of CRF:
1) LHL/Rikshospitalet, Oslo (n=140)
2) St. Olavs University Hospital, Trondheim (n=70)
3) Haukeland University Hospital, Bergen (n=60)
4) Stavanger University Hospital, Stavanger (n=30)

Currently the baseline reference material only contains data of the 70 patients from Trondheim, due to the ongoing COVID-19 pandemic. The testing took place at St. Olavs University Hospital in the NeXt Core Move facility, within four weeks after the screening visit. This was voluntary and they could withdraw at any time, without giving any reason. NorEx was approved by the Regional committee for medical research ethics (2019/797/REK midt), the Norwegian Data inspectorate and the National Directorate of Health and is in compliance with the Helsinki declaration. The study was registered at ClinicalTrials.gov on 05.11.20 (NCT04617639).

Clinical examinations

Height was measured without shoes (Seca 222, Hamburg, Germany). The patient's stood with straight legs, shoulder-width apart, looked straight ahead and height was reported in nearest whole centimetre (without decimal).

Body mass was measured without shoes using the weighing scale Soehnle professional (Svalland AS, Oslo) and was reported to the nearest kilogram (without decimal).

Electrocardiogram (ECG) A standard 12-lead ECG (Custo Cardio 100 BT, Custo Med GmbH, Ottobrunn, Germany) was recorded resting, before starting the 10 min warm-up and during the exercise test, and continued until voluntary exhaustion or stopped due to following: ST depression >2mm (>1 mm if chest pain at the same time), ST elevation >1 mm, arrhythmias: persistent supraventricular tachycardia including atrial fibrillation not present before start of exercise, ventricular tachycardia (>2 ventricular extra heartbeats in series) or increasing ventricular extrasystoles during workload.

Heart rate During the exercise test, the patient's heart rate was measured with the monitor Polar S610i, Polar Electro Oy (Kempele, Finland).

Heart rate recovery was calculated as a decrease in peak HR from peak exercise to 1 min after the exercise test with the patient standing (17).

Blood pressure Just before the warm-up of exercise test and immediately after, blood pressure was measured using an automatic blood pressure monitor (Tango M2, SunTech Medical, Inc., NC, USA) in the exercise lab, NeXt Core Move facility. Blood pressure was measured once in the right arm while standing on the treadmill (postural), with straight legs and with no talking. The left arm was used if the right arm was contraindicated (n=1). HR was also registered with the blood pressure monitor, standing and resting before starting the exercise test (standing HR_{rest}).

Testing of cardiorespiratory fitness

An individualized graded protocol was used. In addition, due to the ongoing pandemic of COVID-19, national and local guidelines were followed during testing, as well as the lab's own routines. The MetaLyzer II (Cortex, Leipzig, Germany) has previously been tested against the Douglas-bag and iron lung (Metabolic Calibration System, VacuMed, Ventura, CA) and were both found reliable and valid (R^2=0.9715). Gas calibrations followed the same protocol as Loe and colleagues (19) with the following modifications: 1) calibration includes measurement of ambient air and a gas mix of known content (15.0 % O_2 and 5.00 % CO_2 in N_2) (Scott medical gases, Netherlands), a calibration of the Triple-V volume transducer with a calibrated 3 L syringe (Calibration syringe C, Medikro Oy, Model: M9474-C, Kuopio, Finland) and barometric pressure control 2) a volume calibration before each test and 3) gas calibration after every third test (19).

The patients were instructed to perform the test on a Woodway treadmill (Weil am Rhein, Germany), unless there were reasons, such as reduced functionality or leg pain, to conduct the test on a stationary cycle ergometer (Lode B.V Medical Technology, Groningen, Netherlands). A control of both velocity and inclination of the treadmill (Bosch DNM 60 L, Professional) was conducted before starting the exercise testing. All patients had an individual warm-up period of 10 minutes where they received detailed instructions about the exercise test and got familiarized with the treadmill. The warm-up workload was based on 1) self-reported physical activity level, 2) monitoring of the HR, and 3) feedback from the patient regarding rate of perceived exertion (moderate intensity), corresponding to 11-13 on the Borg scale. Patients were encouraged to avoid handrail grasp and if necessary, only for maintaining balance. They were instructed to use the same technique (walking or running) during the warm-up and the following test.

Subsequently, the patients wore a face mask (Hans Rudolph, Germany) of appropriate size linked to the MetaLyzer II. After submaximal steady state measurements (see details below), workload was progressively increased about approximately every 90 seconds with 1 km·h^{-1}/2% or a combination of 0.5 km km·h^{-1}/ 1% (treadmill) or 25 W (cycle ergometer) every 30 seconds, respectively. Patients were encouraged to maintain a pedal frequency at approximately 60 rpm. The increase in workload was based on feedback from the patient during the exercise test and physiological responses (HR/VO_2). Based upon testing using this protocol in thousands of individuals at NeXt Core Move facility, we expected for each 1 km·h^{-1}/2% increase in workload, an increase of 3-5 mL·kg^{-1}·min^{-1} in VO_2 and 6-10 beats·min^{-1} increased HR. For the cycle ergometry protocol, years of experience at NeXt Core Move facility has concluded that the used protocol is the one that leads most people close to the true VO_{2max}.

This procedure continued until voluntary exhaustion and the criteria for VO_{2max} were leveling-off VO_2 despite increasing workload; VO_2 does not increase more than 2 mL·kg^{-1}·min^{-1} between two 30-second epochs combined with RER of 1.05 or higher (19) - all other tests were considered as VO_{2peak}. The criteria's for terminating the exercise test were ECG-findings (see clinical examinations), symptoms like chest pain, claudication, extreme fatigue, dizziness or other causes. VO_{2max} was considered as the average of the three highest consecutive 10-seconds measurements of VO_2 with maximal RER considered as the highest measurement that corresponds with the three values off the VO_{2max}. Since 19 of the patients failed to reach VO_{2max}, VO_{2peak} was used.

Borg Scale of Perceived Exertion and VO_2 during CPET

Borg visualizes workload intensity, denoted by numbers 6-20, with a proportional relation between increased rating of perceived exertion and the reported Borg scale number (19,27). Patients were asked to give their subjective rating of perceived exertion during the warm-up at two submaximal levels and after the maximal exercise test. The two submaximal levels were a steady-state measurement and the patients needed to maintain the same workload either on treadmill or cycle ergometer for 2-3 minutes. The VO_2 had to be stable before starting level 2, and if it increased by more than 2 mL·kg^{-1}·min^{-1}, this resulted in waiting another 30 seconds before calculating the average. The calculation was based on the average of four intervals from 2.30 – 3 minutes.
Level 1: The patients had the same workload as the 10 minutes of warm-up.
Level 2: The workload was increased by 1 km·h^{-1} / 2% (treadmill) and 25 W (cycle ergometer). The maximal exercise test started after completing the two submaximal levels.

Physical Activity Index

Patients received a self-administered questionnaire that contained information about the Physical Activity Index (PAI). PAI is found to be a valid and reliable tool to estimate leisure time physical activity (28) and the patients answered three questions with different alternatives. Each answer gave different points and the answers from the three questions were multiplied to find the PAI score. Based on the answers, the patients were categorized to have a physical activity level that corresponded to the following:

1) 0.05 – 1.50 = Low activity
2) 1.51 – 3.75 = Medium activity
3) 3.76 – 15.0 = High activity

Question 1:	**Question 2**:	**Question 3**:
"How frequently do you exercise?"	*"If you exercise as frequently as once or more times a week: How hard do you push yourself?"*	*"How long does each session last?"*
Never [0] <Once a week [0] Once a week [1] 2-3 times a week [2.5] Almost every day [5]	Without breaking a sweat or losing my breath [1] Lose my breath and break into sweat [2] Near exhaustion [3]	<15 minutes [0.1] 15-29 minutes [0.38] 30-60 minutes [0.75] >1 hour [1]

Workload expressed in watts

Workload in watts was calculated at three levels: the two submaximal levels and the maximal exercise test (19). For example: Calculation of watt for a patient at Level 1 (29, s.488): Total vertical distance (velocity · % incline · time) was calculated in order to determine total work, which was then divided by time to provide the workload in watts. Velocity= 5 $km \cdot h^{-1}$/ 3.6 = 1.4 m/s. Incline = 4% = 0.04. Time (t) = 3 min = 180 seconds. Body mass: 109 kg. Total vertical distance: 1.4 m/s · 0.04 % · 180 s = 10.08 m Work (W) = Body mass (kg) · total vertical distance = 109 kg · 9,8 m/s^2 · 10.08 m = 10767.46 Nm. Power = W/t = 10767.46 / 180 s = 59.8 W

The Montreal Cognitive Assessment (MoCA)

MoCA was conducted as a part of another sub-study and is shown to be a simple, reliable and valid test that covers tasks regarding orientation, attention, recall, naming, visuospatial, language and abstract reasoning (30). A meta-analysis has revealed an increased probability for developing cognitive impairment or dementia in post MI patients (31), and the score is from 0-30, where higher score reflects better performance (30).

Allometric scaling

There might be relatively large differences in body mass in post MI patients. Literature has demonstrated that measurements of oxygen uptake in absolute terms ($L \cdot min^{-1}$) or relative to body mass ($mL \cdot kg^{-1} \cdot min^{-1}$) may be imprecise (32). Therefore, it might be necessary to normalize data according to appropriate scaling procedures, to get more accurate comparison of VO_2 between patients with different body mass. The oxygen cost of running at a standard velocity does not increase in direct proportion to body mass, and Helgerud found based on previous literature that comparisons of oxygen uptake should be raised to the power of 0.75 (33). For instance, if not using this dimensional scaling values, light patients would have their VO_{2max} overestimated, compared to heavy patients that would have their VO_{2max} underestimated.

Statistical Analysis

Microsoft Excel version 16 was used to organize data during data collection and the Software program IBM SPSS, version 26 (Statistical Package for Social Science, Chicago, IL) was used for statistical analysis. To determine the association between the physiological variables, linear regression was applied with a 95% confidence interval and a p-value of <0.05 considered statistically significant. GraphPad Prism 9.1.0 (Software, San Diego, California, USA) was used to present the figures and Q-Q plot was used to check for normality distribution. An Independent-Samples T test was utilized to look at level of significance between sexes and the two age groups. All tests were two-sided and Pearson correlations were calculated based on data from Level 1-2 and maximal level. The results are presented as mean ± standard deviations.

Results

A total of 70 Norwegian post MI patients, aged 33-78 yr, had their CRF successfully measured; sixty-nine patients performed the test on the treadmill, and one on cycle ergometer. Descriptive, physiological and cognitive data of the patients are presented in Table 2-4.

Table 2. Descriptive characteristics of post MI patients in NorEx–focus at baseline.

Variables	All (n=70)	Men (n=52)	Women (n=18)
Age (years)	64.6 ± 8.6	65.0 ± 8.5	63.7 ± 9.3
Height (cm)	175.8 ± 8.0	179.2 ± 5.7	165.9 ± 5.2
Body mass (kg)	86.7 ± 14.4	90.5 ± 12.4	75.8 ± 14.5
BMI ($kg \cdot m^{-2}$)	28.0 ± 4.1	28.2 ± 3.6	27.6 ± 5.4
Standing HR_{rest} ($beat \cdot min^{-1}$)	76 ± 14	76 ± 14	77 ± 14
Never smoked (%)	34.3	36.5	27.8
Smoked daily before (%)	44.3	44.2	44.4
Current smoker (%)	7.1	5.8	11.1

n: sample size, BMI: body mass index, standing HR_{rest}: heart rate measured standing before warm-up.

Table 3. Physiological characteristics of post MI patients in NorEx–focus at baseline.

Variables	All (n=70)	Men (n=52)	Women (n=18)
VO_{2peak} ($L \cdot min^{-1}$)	2.60 ± 0.76	2.83 ± 0.71*	1.94 ± 0.51
VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)	30.1 ± 7.9	31.7 ± 7.9*	25.7 ± 6.1
VO_{2peak} ($mL \cdot kg^{-0.75} \cdot min^{-1}$)	91.5 ± 24.1	97.0 ± 23.7*	75.5 ± 17.7
Peak O_{2pulse} ($mL \cdot beat^{-1}$)	16.5 ± 4.4	18.0 ± 3.9*	12.5 ± 2.9
RER ($CO_2 \cdot VO_2^{-1}$)	1.07 ± 0.06	1.07 ± 0.06	1.08 ± 0.07
Workload ($Watt_{peak}$)	161 ± 56	178 ± 52*	112 ± 32
BORG	19 ± 1	19 ± 1	19 ± 1
HR recovery, 1 min ($beat \cdot min^{-1}$)	27.9 ± 12.1	28.4 ± 13.2	26.5 ± 8.5
Pre exercise postural BP (mmHg)	152/92	151/92	157/92
Post exercise postural BP (mmHg)	176/105	176/105	186/106
HR_{peak} ($beat \cdot min^{-1}$)	157 ± 17	158 ± 17	156 ± 20

Data are presented as mean ± standard deviation. *Significant difference between sex $p<0.05$, VO_{2peak}: peak oxygen uptake, Peak O_{2pulse}: oxygen uptake per heartbeat, an indirect reflection of left ventricular stroke volume, CO_2: Carbon dioxide, RER: respiratory exchange ratio, Workload: peak treadmill/cycle ergometer exercise load, BORG: subjective perception of fatigue at VO_{2peak} (6-20), HR recovery: heart rate recovery 1 minute after peak heart rate, reflects reactivation of the parasympathetic nervous system, Pre exercise postural BP: blood pressure taken standing before warm-up, BP: blood pressure - systolic/diastolic (mmHg), Post exercise postural BP: blood pressure taken immediately after maximal test, HR_{peak}: peak heart rate. Missing information (number of patients): Peak O_{2pulse}: n=4.

Table 4. Physiological and cognitive variables of patients in NorEx–focus stratified by sex and age.

Variables	<65 yr Men (n=24)	$\geq$ 65 yr Men (n=28)
VO_{2peak} ($L\cdot min^{-1}$)	3.27 ± 0.70#	2.45 ± 0.45
VO_{2peak} ($mL\cdot kg^{-1}\cdot min^{-1}$)	34.8 ± 8.0#	28.8 ± 6.9
VO_{2peak} ($mL\cdot kg^{-0.75}\cdot min^{-1}$)	108.3 ± 23.8#	87.4 ± 19.2
Body mass (kg)	94.7 ± 11.6#	86.9 ± 12.0
Height (cm)	180 ± 6	179 ± 6
RER ($CO_2\cdot VO_2^{-1}$)	1.08 ± 0.07	1.05 ± 0.05
HR_{peak} ($beat\cdot min^{-1}$)	161 ± 16	155 ± 18
HR recovery, 1 min ($beat\cdot min^{-1}$)	29.8 ± 12.0	27.3 ± 14.2
Workload ($Watt_{peak}$)	201 ± 58#	158 ± 37
BORG	19 ± 1	18 ± 1
Physical Activity Index score	4.46 ± 2.39	4.50 ± 2.75
MoCA Score	26.0 ± 2.7	25.0 ± 2.8
Variables	**<65 yr Women (n=9)**	**$\geq$65 yr Women (n=9)**
VO_{2peak} ($L\cdot min^{-1}$)	2.17 ± 0.43	1.72 ± 0.51
VO_{2peak} ($mL\cdot kg^{-1}\cdot min^{-1}$)	27.5 ± 5.6	23.9 ± 6.4
VO_{2peak} ($mL\cdot kg^{-0.75}\cdot min^{-1}$)	81.6 ± 15.0	69.4 ± 18.9
Body mass (kg)	80.3 ± 17	71.2 ± 10.4
Height (cm)	165.7 ± 6	166 ± 5
RER ($CO_2\cdot VO_2^{-1}$)	1.06 ± 0.07	1.09 ± 0.07
HR_{peak} ($beat\cdot min^{-1}$)	162 ± 20	151 ± 20
HR recovery, 1 min ($beat\cdot min^{-1}$)	26.7 ± 7.0	26.2 ± 10.3
Workload ($Watt_{peak}$)	117 ± 37	107 ± 28
BORG	18 ± 1	19 ± 1
Physical Activity Index score	4.31 ± 2.06	3.54 ± 1.85
MoCA score	25.7 ± 2.8	24.0 ± 4.5

Data are presented as mean ± standard deviation. n: sample size, #significant difference between age groups, VO_{2peak}: peak oxygen uptake, CO_2: Carbon dioxide, RER: respiratory exchange ratio, HR_{peak}: peak heart rate, HR recovery: heart rate recovery 1 minute after peak heart rate, reflects reactivation of the parasympathetic nervous system, Workload: peak treadmill/cycle ergometer exercise load, BORG: subjective perception of fatigue (6-20) at VO_{2peak}, MoCA score: 0-30 points, Physical Activity Index score: A weighted product score between training – intensity, duration, and frequency. Missing information (number of patients): Physical Activity Index score: n=6.

Cardiorespiratory fitness

Overall, VO_{2peak} was 2.60 ± 0.76 L·min^{-1} or 30.1 ± 7.9 mL·kg^{-1}·min^{-1} (range 8.9– 49.9 mL·kg^{-1}·min^{-1}, Table 3). The patient that performed the CRF test on cycle ergometer (woman, age: 66 yr), had a VO_{2peak} of 1.55 L·min^{-1} or 23.2 mL·kg^{-1}·min^{-1}. The highest observed VO_{2peak} was observed in men and women aged <65 yr (sex differences, p<0.16) (Table 4). VO_{2peak} in men aged <65 yr were 25% (p<0.001), 17% (p<0.005), and 19% (p<0.001) higher compared with those aged ≥65 yr when expressed in absolute terms (L·min^{-1}), directly relative to body mass (mL·kg^{-1}·min^{-1}) and when using appropriate scaling procedures (mL·kg^{-75}·min^{-1}), respectively (Table 4). The corresponding values for women aged <65 yr were 21% (p=0.063), 13% (p=0.222), and 15% (p=0.149) higher compared with those aged ≥65 yr. Women had 22.2% lower VO_{2peak} (mL·kg^{-1}·min^{-1}) when compared with men when using appropriate scaling procedures (p<0.001).

Heart rate, Borg scale and Cardiorespiratory fitness

Overall, standing HR_{rest} was 76 ± 14 beat·min^{-1} and HR_{peak} 157 ± 17 beat·min^{-1} (no significant age group or sex differences). Borg scores were 19 ± 1 in both sexes after the maximal exercise test (no significant age group or sex differences) (Table 3). There were no differences between sexes in rating of perceived exertion in relation to both $\%HR_{peak}$ and $\%VO_{2peak}$ (Table 5). For example, the actual exercise intensity for men and women that report to exercise at Borg 10-12 corresponds to 73.5% (CI: 69.6-77.5) and 75.0% (CI: 72.0-78.0) of HR_{peak}, respectively (sex differences, p=0.70).

Heart rate recovery

The highest heart rate recovery was observed among both men (29.8 ± 12.0 vs. 27.3 ± 14.2 beat·min^{-1}, p=0.493) and women <65 yr (26.7 ± 7.0 vs. 26.2 ± 10.3 beat·min^{-1}, p=0.895) compared with ≥65 yr. There were no significant differences in HR recovery between sexes (p=0.566).

Table 5. Relationships between perceived exertion, oxygen uptake and HR in post MI patients.

	All			Men			Women		
Borgscale	**%HR_{peak}**	**95% CI**	**n**	**%HR_{peak}**	**95% CI**	**n**	**%HR_{peak}**	**95% CI**	**n**
6-9	70.5	-	1	70.5	-	1	-	-	-
10-12	73.8	70.6-77.0	45	73.5	69.6-77.5	36	75.0	72.0-78.0	9
13-15	77.1	74.9-79.3	83	76.6	74.0-79.3	59	78.1	73.9-82.3	24
16-18	95.8	93.1-98.4	37	95.7	92.8-98.7	26	95.9	89.6-102.2	11
19+	100	100-100	44	100	100-100	34	100	100-100	10
Borgscale	**%VO_{2peak}**	**95% CI**	**n**	**%VO_{2peak}**	**95% CI**	**n**	**%VO_{2peak}**	**95% CI**	**n**
6-9	57.0	-	1	57.0	-	1	-	-	-
10-12	57.6	54.2-61.1	45	56.8	52.7-60.9	36	60.8	54.5-67.1	9
13-15	65.7	62.9-68.5	82	64.7	61.3-68.1	59	68.1	63.4-72.8	24
16-18	93.2	89.3-97.0	37	93.1	88.5-97.8	26	93.2	85.3-101.1	11
19+	100	100-100	44	100	100-100	34	100	100-100	10

n: sample size, Borgscale: subjective perception of perceived exertion at two submaximal and maximal level (6-20), CI: confidence interval, %HR_{peak}: percentage of peak heart rate, %VO_{2peak}: percentage of peak oxygen uptake, -: option not chosen.

Figure 2 demonstrates the relationship between VO_2 and HR. The overall correlation for VO_2 ($L \cdot min^{-1}$) and HR was found to be strong (r=0.69, p<0.001). Stratified by sex, this correlation became stronger; men r=0.74 (p=0.001), women r= 0.76 (p<0.001). The correlation between $\%VO_2$ and $\%HR_{peak}$ was strong; all r =0.92 (p<0.001), men r=0.93 (p<0.001), women r=0.89 (p<0.001).

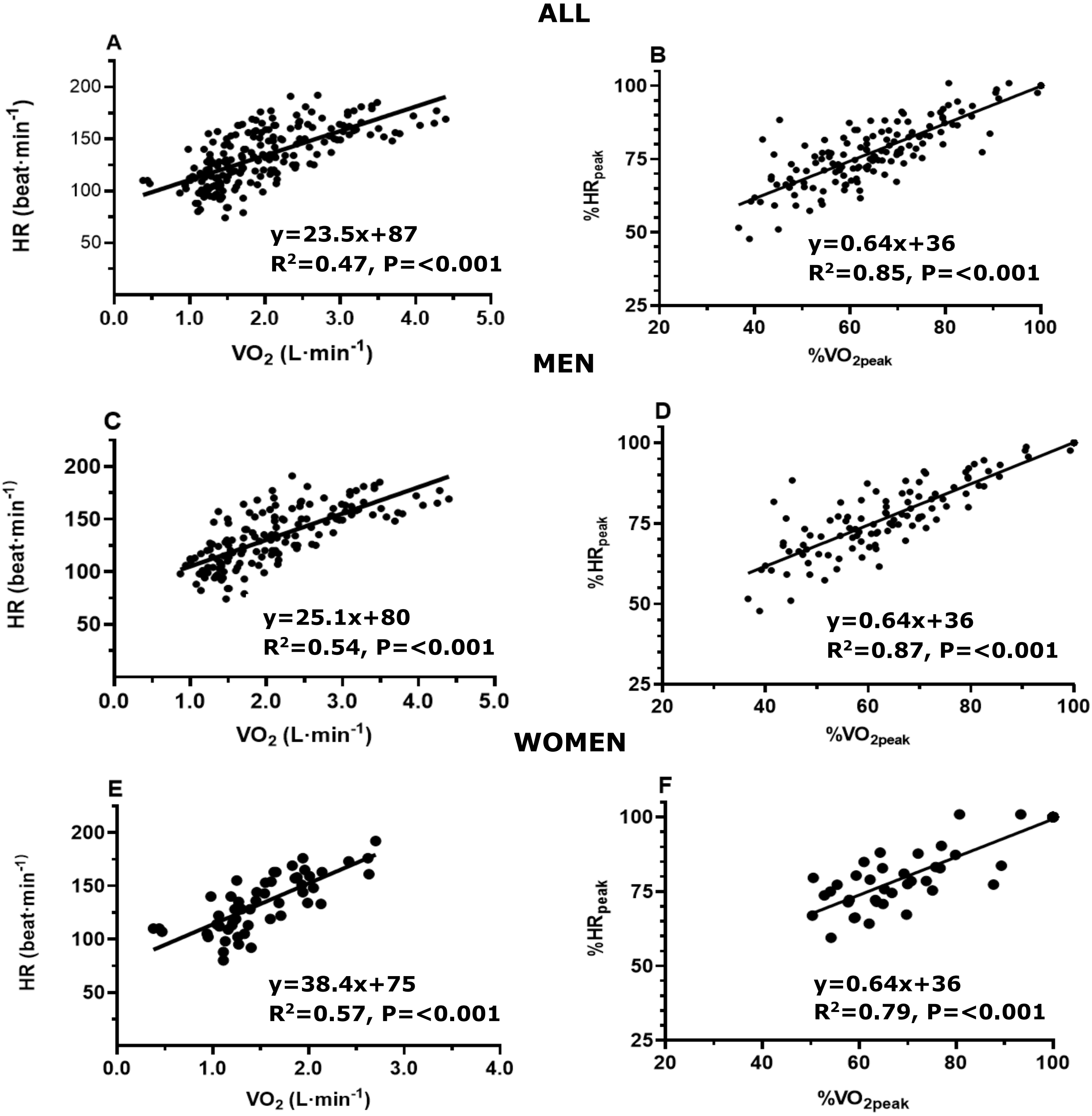

Figure 2. Correlations between oxygen uptake (VO_2) and heart rate (HR).

Oxygen pulse

Overall, peak O_{2pulse} was 31% lower in women than men (12.5 ± 2.9 mL·beat^{-1} vs. 18.0 ± 3.9 mL·beat^{-1}) ($p<0.001$). When dividing into age groups, women had 33% and 28% ($p<0.001$) lower peak oxygen pulse when compared to men in the age group <65 yr and ≥65 yr (Table 6). The highest peak O_{2pulse} was observed among both men (20.3 ± 3.8 mL·beat^{-1} vs. 13.6 ± 1.8, $p<0.001$) and women (13.6 ± 1.8 mL·beat^{-1} vs. 11.4 ± 3.4, $p=0.119$) aged <65 yr compared with ≥65 yr.

Men <65 yr had 4.4 mL·beat^{-1} higher peak O_{2pulse} compared with men ≥65 yr ($p<0.001$). A 2.2 mL·beat^{-1} higher peak O_{2pulse} was observed in women <65 yr compared to women ≥65 yr ($p=0.228$) (Table 6). At submaximal levels, men <65 yr had 3.7 mL·beat^{-1} higher O_{2pulse} at both Level 1 and 2 ($p<0.001$). The corresponding values for women were 2.3 mL·beat^{-1} ($p<0.034$), and 2.2 mL·beat^{-1} ($p=0.84$) higher O_{2pulse} compared with women aged ≥65 yr.

Table 6. O_{2pulse} of patients in NorEx–fokus stratified by intensity levels, sex and age groups.

<65 years	**Men (n=24)**			**Women (n=9)**		
	Level 1	**Level 2**	**Maximal**	**Level 1**	**Level 2**	**Maximal**
O_{2pulse} (mL·beat^{-1})	16.0 ± 3.1$^{\#*}$	16.9 ± 3.4$^{\#*}$	20.3 ± 3.8$^{\#*}$	11.4 ± 1.7$^{\#}$	11.9 ± 2.4	13.6 ± 1.8
VO_{2peak} (mL·kg^{-1}·min^{-1})	19.9 ± 5.9	22.8 ± 6.4	34.8 ± 8.0$^{\#}$	16.8 ± 4.2	19.5 ± 4.8	27.5 ± 5.6
$\%VO_{2peak}$	57.9 ± 12.7	66.1 ± 13.4		61.3 8 ± 8.5	71.2 ± 10.4	
$\%HR_{peak}$	71.6 ± 11.1	78.6 ± 11.3		71.5 ± 6.7	79.3 ± 8.6	
Workload (watts)	47 ± 21	75 ± 25	201 ± 58$^{\#*}$	28 ± 12	44 ± 15	117 ± 37
≥65 years	**Men (n=28)**			**Women (n=9)**		
O_{2pulse} (mL·beat^{-1})	12.3 ± 2.4*	13.2 ± 3.0*	15.9 ± 2.6*	9.1 ± 2.5	9.7 ± 2.7	11.4 ± 3.4
VO_{2peak} (mL·kg^{-1}·min^{-1})	16.9 ± 5.1	19.7 ± 6.4	28.8 ± 6.9	14.5 ± 3.0	16.9 ± 4.3	23.9 ± 6.4
$\%VO_{2peak}$	59.0 ± 11.7	68.4 ± 14.2		63.0 ± 12.2	72 ± 8.6	
$\%HR_{peak}$	74.2 ± 9.5	77.5 ± 18.1		76.6 ± 10.1	84.1 ± 7.6	
Workload (watts)	32 ± 13	54 ± 14	158 ± 37*	27 ± 14	39 ± 17	107 ± 28

Data are presented as mean ± standard deviation. n: sample size, $^{\#}$significant difference between age groups, *significant differences between sex, O_{2pulse}: oxygen uptake per heartbeat, an indirect reflection of left ventricular stroke volume, VO_2: oxygen uptake, $\%HR_{peak}$: percentage of peak heart rate, Workload: treadmill/cycle ergometer exercise load at sub and maximal workload. Missing information (number of patients): Level 1 O_{2pulse} n=1, Level 2 O_{2pulse} n=2, Maximal O_{2pulse} n=4, $\%HR_{peak}$ n=1.

Watt, Heart Rate and Cardiorespiratory fitness

Figure 3 presents the correlation between VO_2 ($L\cdot min^{-1}$) and treadmill/cycle ergometer workload (watts) with a strong association for all, r=0.80 ($p<0.001$). Stratified by sex, strong correlations were also observed in men, r=0.80 ($p<0.001$) and women, r=0.69 ($p<0.001$). The figure also demonstrate the correlation between HR and Watts with strong correlation overall r=0.65 ($p<0.001$). Stratified by sex, strong correlations were also observed in men, r=0.68 ($p<0.001$) and women, r=0.67 ($p<0.001$).

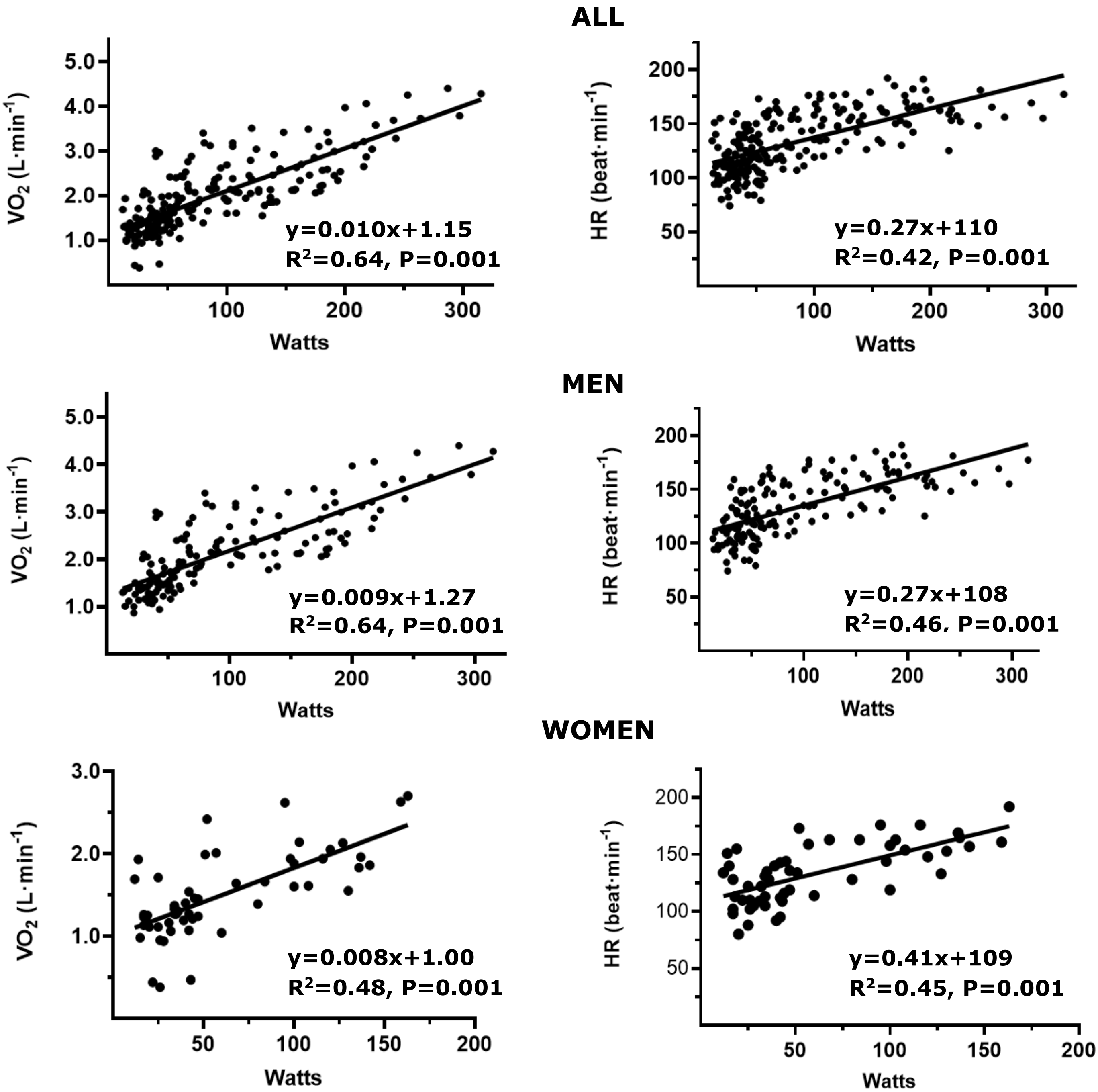

Figure 3. Correlations between workload (Watts) and oxygen uptake (VO_2) and correlations between Watts and heart rate (HR).

The Montreal Cognitive Assessment (MoCA)

We observed overall MoCA score of 25.3 ± 3.0 points; men 25.5 ± 2.8 points (range 19-30 points) and women 24.8 ± 3.7 points (range 13-29 points). The highest score was observed in men (26.0 ± 2.7, p=0.168), and women <65 yr (25.7 ± 2.8 points, p=0.359), respectively.

Physical Activity Index

Overall, the physical activity index score was 4.33 ± 2.41 points. The highest score was observed in men ≥65 yr and women <65 yr with the scores of 4.50 ± 2.75 and 4.31 ± 2.06 (no significant difference between age groups) which indicate a level of high physical activity (no significant sex differences).

Table 7. Physical activity data results of post MI patients in NorEx–focus at baseline.

	All (n=64)	**Men (n=46)**	**Women (n=18)**
Frequency	**n / %**	**n / %**	**n / %**
Never	-	-	-
Less than once	1 (1.6)	1 (2.2)	-
Once a week	6 (9.4)	6 (13.0)	-
2-3 times a week	44 (68.8)	29 (63.0)	15 (83.3)
Almost every day	13 (20.3)	10 (21.7)	3 (16.7)
Intensity			
Take it easy	12 (18.8)	6 (13.0)	6 (33.3)
Heavy breath and sweat	51 (79.7)	39 (84.8)	12 (66.7)
Near exhaustion	1 (1.6)	1 (2.2)	-
Duration			
Less than 15 min	-	-	-
15-29 min	6 (9.4)	5 (10.9)	1 (5.6)
30-60 min	34 (53.1)	20 (43.5)	14 (77.8)
> 1 hour	24 (37.5)	21 (45.7)	3 (16.7)
Physical Activity Index score	4.33 ± 2.41	4.48 ± 2.57	3.93 ± 1.93

Data are presented as mean ± standard deviation. n:sample size, Physical Activity Index score: A weighted product score between training- intensity, duration and frequency, -:option not chosen. Missing information (number of patients): Physical Activity Index score: n=6.

Figure 4 illustrate a poor, but statistically significant association between physical activity index score and VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$), all $r=0.25$ ($p<0.050$). In men, we observed a weak correlation, $r=0.19$ ($p=0.213$) and in women, a moderate correlation $r=0.40$ ($p=0.104$).

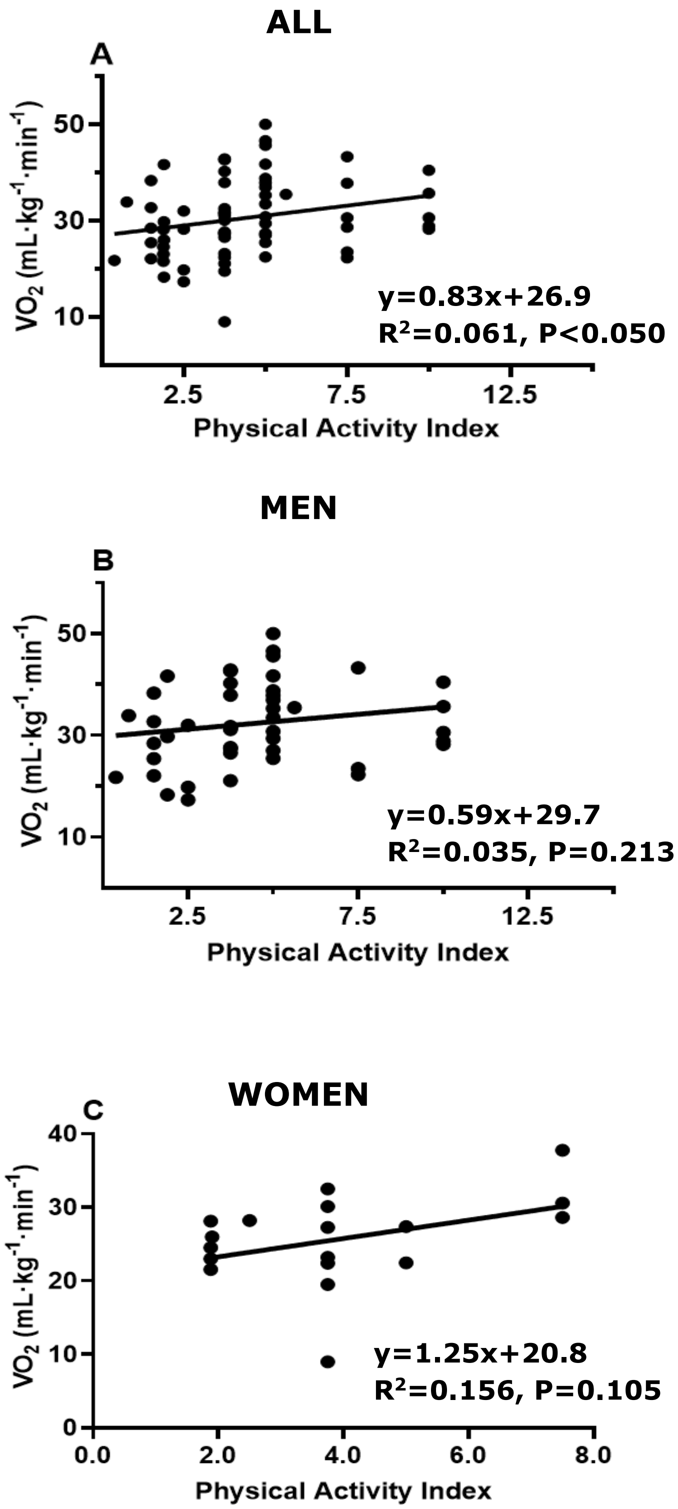

Figure 4. Correlations between physical activity index score and oxygen uptake (VO_2).

Discussion

This is the start of a valid reference material of objectively measured CRF and cardiovascular physiology data on Norwegian post MI patients. In the future, this data may improve diagnostics and be an important tool for both prevention and treatment in post MI patients. The major limitations with exsisting studies includes not using CPET for testing of CRF, using cycle ergometry as method, the lack of women, and none of them have actually had the aim to provide reference material (3,5,7,13,15,26). Interestingly, 52 of 70 MI were men and a report of AHA regarding heart disease statistics from 2016 demonstrate that women may experience MI at a later age (34,35). Although underrepresented in this study, a larger number of women will contribute to the reference material in different age groups after 3.5 years.

Cardiorespiratory fitness

The overall VO_{2peak} of 30.1 ± 7.9 $mL \cdot kg^{-1} \cdot min^{-1}$ is in line with former Norwegian studies measuring CRF with CPET (range 31.8 – 32.2 $mL \cdot kg^{-1} \cdot min^{-1}$) (23,24). The importance of acknowledging the extreme outlier in women of 8.9 $mL \cdot kg^{-1} \cdot min^{-1}$ or 0.47 $L \cdot min^{-1}$ impacts the results, and the overall VO_{2peak} would have been 30.4 $mL \cdot kg^{-1} \cdot min^{-1}$ or 2.63 $L \cdot min^{-1}$ when excluding data from this patient. For women, the VO_{2peak} would be 26.6 $mL \cdot kg^{-1} \cdot min^{-1}$ or 2.03 $L \cdot min^{-1}$. Two studies of Keteyian et al. (4,25) demonstrated VO_{2peak} ranging from 14.8 ± 4.2 $mL \cdot kg^{-1} \cdot min^{-1}$ to 22.4 $mL \cdot kg^{-1} \cdot min^{-1}$, which is lower than the findings in this study. Kavangah et al. (6) observed a mean VO_{2peak} of 15.4 ± 4.0 $mL \cdot kg^{-1} \cdot min^{-1}$ in women testing CRF on cycle ergometer. This study only had one cycle ergometry test (23.2 $mL \cdot kg^{-1} \cdot min^{-1}$), which makes it difficult to compare this result on a general basis. Women had 31% and 19% lower absolute ($L \cdot min^{-1}$) and relative ($mL \cdot kg^{-1} \cdot min^{-1}$) VO_{2peak}, which is in accordance with data from Trøndelag Health Study (HUNT) in healthy matched peers (19). When comparing the dimensional scaling values of VO_2, women had 22.2 % lower VO_{2peak} ($mL \cdot kg^{-0.75} \cdot min^{-1}$). Nevertheless, the present study has a majority of men and there is a need to have more data on VO_{2peak} on women to have a better comparison of VO_{2peak} relative to dimensional scaling values ($mL \cdot kg^{-0.75} \cdot min^{-1}$). The observed differences in VO_{2peak} between sexes are expected due to several factors, such as larger hemoglobin concentration, muscle mass and stroke volume in men (36).

When comparing with HUNT from Loe et al. (19) on a healthy Norwegian population aged 20-90 yr that performed CPET measurements on treadmill, 9 of 70 MI patients had higher VO_{2peak} compared to healthy individuals at their age and sex. This demonstrates that improving VO_{2peak} is still possible after MI and a large amount of men and women had values close to the average VO_{2peak} matched with peers from HUNT, enhancing the importance of being regular physically active. The reason for why these post MI patients have a higher VO_{2peak} is difficult to determine, but six demonstrated a physical activity index score higher than the average (5.69 ± 2.18 vs. 4.48 ± 2.57 points), which indicates an active population. For women, one had higher VO_{2peak}, whereas seventeen had VO_{2peak} lower than age and sex matched healthy peers from HUNT (19) (range 0.2 - 22.1 $mL \cdot kg^{-1} \cdot min^{-1}$). The corresponding values for men were; eight had higher VO_{2peak} (range 0.6 – 7.4 $mL \cdot kg^{-1} \cdot min^{-1}$), whereas forty-four had VO_{2peak} lower (range 0.5 -20.9 $mL \cdot kg^{-1} \cdot min^{-1}$), respectively.

Despite having a similar mean VO_{2peak} compared with previous Norwegian studies of post MI patients (23,24), a total of 19 men age 42-75 yr displayed values 10.3 – 20.9 $mL \cdot kg^{-1} \cdot min^{-1}$ below the average VO_{2peak} compared to healthy individuals from HUNT (19). Numerous studies have demonstrated that 1-MET higher CRF is associated with improved survivability (2,3). Multiple studies have also reported the importance of improving or maintaining a good CRF level to protect against cardiovascular mortality (2,3,7). Creating this reference material on post MI patients may therefore encourage people to improve their CRF and be more physically active. Surprisingly, by comparing our MI patients with the reference material on CRF in USA, age 20-90 yr on apparently healthy population (8), our MI patients, both men and women had generally higher VO_{2peak}. However, it is challenging to compare VO_{2peak} results among countries. Peterman et al. (37) reported that methodological limitations may affect comparison of CRF, and the need of enhancing a global registry of CRF data to reduce potential bias and to improve international comparisons. These methodological factors can be sample size, protocols used for exercise testing, CPET equipment, cycle ergometer vs. treadmill or data collection methods.

After 3.5 yr, this material may influence clinical decisions. For example, can a low VO_{2peak} be used to trigger more aggressive clinical management, and therefore reduce death and hospitalizations? (18). Furthermore, in a few years this material could provide expected normal CRF values of men and women for all age groups with MI. This could lead to a more accurate assessment of the impact of CRF on health outcomes. For instance, Kokkinos and colleagues (38) have stated that the risk associated with 5 MET achieved by a 40 yr old cannot be comparable with a 70 year old attaining the same MET level. This may provide personalization of exercise prescription, optimize survival, secondary prevention and functional outcomes (39).

Heart rate, Borg Scale and Cardiorespiratory fitness

Standing HR_{rest} of 76 ± 14 beat·min^{-1} is in contrast with some studies of post MI-, CVD patients (23,24,40), but in line with other studies including post MI patients (3,4,41). Most importantly, these studies have measured resting HR (HR_{rest}). For example, two of these studies had patients resting for either 10 minutes or 5 min in a chair (24,40). In contrast, our measurements were performed in the exercise lab with several disturbing factors, which may explain why the HR is approximately 10-18 beat·min^{-1} higher in our study. This also applies to the blood pressure measurements with only one measurement, resulting in approximately 24 mmHg higher values compared to previous studies (23,40). The overall HR_{peak} of 157 ± 17 beat·min^{-1} is in line with previous research on post MI patients (range 153-156 beat·min^{-1}) (23,24). Still, these studies consisted mainly of men and in a few years the final reference material would be able to present HR_{peak} variations in both sexes and the distribution by age groups. Additionally, our post MI patients had a lower average HR_{peak} compared to healthy matched peers in HUNT (19). This may be explained by medication use that can lower both HR and HR_{peak} during exercise (11).

We observed remarkably lower %VO_{2peak} and %HR_{peak} for Borg score at lower intensities for both men and women, compared with both Loe et al. (19) in healthy individuals and Stensvold et al. (40) in a general population of older adults. For example, men had an average of 73.5 vs. 78.1 %HR_{peak} at Borg score 10-12 and women had 75.5 vs. 82.2 %HR_{peak} compared to HUNT (19). At higher Borg levels (>16), %HR_{peak} were similar for both sexes. This indicates that MI patients in this study report a higher rating of perceived exertion at lower intensities than the actual workload suggests. Moholdt et al. (42) demonstrated that using Borg scale with the aim to exercise at HR_{peak} at 85-95% was not adequate for exercise prescription in CR, and that rating of perceived exertion corresponds to lower HR. Borg scale has been reported to be an important tool for guiding exercise intensity and may be used instead of heart rate monitors (27). It may be that our MI patients were not familiar with the use of Borg Scale. However, it could also be that there is a need to establish new relationships between Borg scale and intensity for post MI patients, and this study can help to clarify this.

Comparing the present results to a study of Choe et al. (41) with 66 post MI patients (aged 56.7 ± 9.5 yr), a significant correlation was also found between VO_2 and HR. The observed association between percentage VO_{2peak} and percentage HR_{peak} frequencies in this current study, showed that at 50, 70 and 80%VO_{2peak}, the %HR_{peak} values were on average 68, 80, 87%, respectively. These results showed 6-10% higher HR_{peak}, compared with the American College of Sports Medicine (ACSM) guidelines on a healthy population (43). This is in agreement with a study of Stensvold et al. (40) that stated "… *it is a greater physiological cost to work at higher intensities for people with CVD*".

Byrne and Hills (43) also reported a higher %HR_{peak} at given %VO_{2peak} in obese men and women (aged 42.1 ± 9.6 yr). The literature outlined the weakness of ACSM guidelines of pooling raw data to produce a single group regression resulting in removing of individual variability and that using %HR_{max} at given proportions is mathematically unsound. The strong association between %HR_{peak} and %VO_{2peak} is in agreement with the findings in Loe et al. (19), and Choe et al. (41). This study also revealed a stronger correlation over time, after MI. Interestingly, the HERITAGE Family Study (44) demonstrated that a 20-week exercise program did not affect HR at given %VO_{2max} in both men and women aged 17-65 yr, proving that HR is a good estimate of relative exercise intensity, which can be an important tool in an exercise program. Furthermore, this indicates that testing CRF frequently with CPET is not necessary to adjust the exercise prescription.

Heart rate recovery

In Norwegian post MI patients aged 57.4 ± 9.5 yr, Moholdt et al. (24) found an HR recovery of 31.4 ± 9.4 beat·min^{-1} in patients performing 4x4 intervals and 32.6 ± 9.5 beat·min^{-1} in the usual care aerobic group, which is slightly above the findings in this study. This may be explained by a higher VO_{2peak} and younger age in the Moholdt study. The Generation 100 study which included older CVD patients found a HR recovery of 25 ± 10 beat·min^{-1} in women (n=93) and 27 ± 12 beat·min^{-1} in men (n=205), that is very similar to our findings (40). Two patients in this study had HR recovery <12 beat·min^{-1}, which is related to increased risk of premature death (17,40). Still, the mean HR recovery indicates that post MI patients in the current study do not have a delayed decrease in HR after exercise (40).

Oxygen pulse

An outlier in O_{2pulse} was observed in women $\geq$65 yr with a decrease in VO_2 after Level 2, despite increased workload and RER-value of 1.0. If this data was taken out of the analysis, the results would have been 9.8 ± 3.4 mL·beat^{-1} in Level 1, 10.4 ± 1.7 mL·beat^{-1} in Level 2, and 12.4 ± 2.1 mL·beat^{-1} at Maximal Level. Overall peak O_{2pulse} for women $\geq$65 yr and both sexes would have been 13.0 ± 2.0 mL·beat^{-1} and 16.7 ± 4.1 mL·beat^{-1}, respectively. The SAINTEX-CAD study (45) included 200 patients aged 40-75 yr (180 men, 20 women) and 115 of them had post MI. The results showed a peak O_{2pulse} of 14.8 ± 3.6 mL·beat^{-1} and 14.7 ± 2.9 mL·beat^{-1} in patients randomized for high intensity aerobic intervals or aerobic continuous training before starting the intervention. The Generation 100 study demonstrated a peak O_{2pulse} of 11.1 ±2.9 mL·beat^{-1} in 93 women and 16.3 ± 8.5 mL·beat^{-1} in 205 men with CVD, which is both slightly under the finding in this study. The reason for this might be age, mixed CVD or exercise- and lifestyle habits.

When comparing our MI patients with healthy men and women from HUNT (19), peak O_{2pulse} were quite similar in both sexes and age groups. However, these results need to be evaluated with caution due to a large variation in age in both groups and sexes. Nonetheless, the results reflects a normal stroke volume response to exercise in our post MI patients (40). According to AHA (11), O_{2pulse} increases rapidly during the initial stages of exercise with a slow approach at the end of exercise test. This is in line with the submaximal levels results of O_{2pulse} in both sexes and age groups, demonstrating a progressively higher O_{2pulse} during exercise testing. In the future, this O_{2pulse} data can be important for improving test interpretation, since it reflects cardiac function and could help make a better assessment of prognosis and detect several diseases (11).

Watt, Heart Rate and Cardiorespiratory fitness

To my knowledge there exists few studies demonstrating the association between HR and watts or VO_2 ($L \cdot min^{-1}$) vs. watts in post MI patients. For patients where CPET testing is not available, watt can be used to estimate CRF based on speed, incline and duration of the treadmill or cycle ergometry workload (2). In this study, both men and women <65 yr with highest HR_{peak} and VO_{2peak} achieved greater watts (Table 4). For patients, the use of HR and watts can be used to demonstrate improvements in CRF either on treadmill or cycle ergometer. For instance, our post MI patients test their CRF with CPET before and after CR program. The VO_2 ($L \cdot min^{-1}$) at given intensities can give additional information about improvements in CRF such as lower oxygen cost and HR at submaximal levels, as indicated in the study of Wisløff et al. (46).

The Montreal Cognitive Assessment (MoCA)

A previous study has demonstrated that there exist little comparative data on cognitive function and post MI patients (47). However, a systematic review found that MI was associated with 45 % increased risk of cognitive impairment, cognitive decline, or dementia (31). The question of what causes the increased risk of dementia in MI- and CVD patients is still unanswered (31,47). Based on normative MoCA data on the Swedish population aged 65-85 yr (48), MoCA cut-offs (1-2 standard deviation) for cognitive impairment ranged from <25 to <21 for the lowest educated and <26 to <24 for the highest educated, depending on age group. This indicates that our MI patents are between normal cognitive function and mild cognitive impairment. However, the results should be evaluated with caution due the large variation in age with and lack of information on education. In the future, it will be interesting to examine differences in MoCA score between sex and age group distribution.

Physical Activity Index

There was an overall poor correlation (r=0.25) between self-reported physical activity level and VO_2, which indicates that only 6.1 % of differences in VO_{2peak} can be explained by differences in PAI scores, which is in agreement with the study of Loe et al. (19). Since the PAI score is based on the answers regarding duration, frequency and intensity of exercise, it might be that the MI patients underestimate the intensity level while exercising or are not aware of their own physical activity habits. Still, it will be interesting to see the association between these variables when more MI patients are included. This self-reported questionnaire on physical activity could be an important tool for predicting CRF, where other measurements could be more costly, time-consuming, and not feasible (49). Kurtze et al. (28) found a moderate and significant correlation (r=0.48) between PAI score and direct measurement of VO_{2max} in healthy aged 40 yr, which is in contrast to our finding and indicates that PAI in post MI patients is not considered as a reliable tool for estimating leisure time physical activity.

Interestingly, MI patients in this study reported a higher overall PAI score vs. healthy Norwegian individuals (19) (4.33 ± 2.41 vs. 3.41 ± 2.88 points). This may be explained by a much smaller sample size, where some high scores may increase the average score substantially. The highest VO_{2peak} measurements were observed in men and women <65 yr. This result fits with women <65 yr who had higher level of physical activity compared to the older age group. Still, men $\geq$65 yr had a lower VO_{2peak}, but a higher level of physical activity. This could be explained by a larger sample size (20 vs. 26). Men and women with the highest VO_{2peak} (mL·kg^{-1}·min^{-1}) had 8% and 13% higher body mass, respectively. By analysing the results, sixteen men <65 yr were $\geq$90 kg vs. eleven in patients $\geq$65 yr. For women <65 yr five were $\geq$80 kg vs. one $\geq$65 yr. Those with a higher body mass did not have particularly lower VO_{2peak} compared to the older age group. This indicates that patients with a higher body mass still maintain a high level of physical activity.

Interestingly, only 1 of 70 patients reported to exercise near exhaustion during leisure time physical activity (Table 7). This may be explained by numerous factors such as fear of exercising with high intensity after MI, pain or fatigue (39). Additionally, such factors could therefore explain why the preferable exercise choices were moderate intensity with duration of 30-60 minutes and >1 hour. Studies have shown that high intensity training is more effective than moderate intensity to improve VO_{2peak} (23,24) and considering this, a larger amount of patients could have demonstrated higher VO_{2peak}, exercising with less duration and with higher intensity, but this remains speculative at current in our population.

Strength and Limitations

The main strength of this study is the broad inclusion criteria and few exclusion criteria. HUNT (50) demonstrated that Trøndelag is representative for the population of Norway, and the results in this study can therefore likely be transferred to the extended Norwegian MI-population. This assumption will be tested when CPET will be undertaken in MI-patients throughout Norway when COVID-restrictions allows for that. Another major strength is that all the objective exercise tests were performed in the same lab, NeXt Core Move facility and by the same two exercise physiologists students, which could evaluate the criteria for a true VO_{2max} test. Furthermore, this material on CRF was performed on treadmill (cycle ergometer n=1) and by using the gold standard for objectively testing of CRF (2,3). For exercise testing, 1.5 hour was scheduled for each MI patient, with enough time to give a detailed explanation of the testing procedure and purpose, and information about possible symptoms and complications (11). The ECG signal can make noise produced by electrodes or cable movement (11) , and therefore a heart rate monitor was used in addition to ensure that variables such as HR_{peak} and HR recovery were measured accurately.

The MI patients were recruited through the MI-registry and perhaps the most fit patients are more willing to participate and therefore complete exercise testing, contributing to bias. This study did not have information about comorbidities, medication use, mental health, when and how many MI patients had during the last years, which could be used to get more insight into the VO_{2peak}, HR_{peak} or other results, and therefore finding out what characterizes this population. Furthermore, the sample size in women (n=18) was small, and this study was not able to divide the sample size into several age groups such as Loe et al. (19), which is the overall aim of this reference material.

An interesting topic for future work on this data material could therefore be to gather more information about the patient's comorbidities, body composition, disease history, education and mental health to find out what characterizes those who exercise often after a first MI, and those who exercise less. As stated by Kaminsky et al. (10) *"…future* *work should explore the contribution of each of these factors to the change in CRF as it relates to predicting health-related outcomes"* (10).

Conclusion

This study is a start of a valid reference material on objectively measured CRF and cardiovascular physiology data on post MI patients. This data will create normal values for the key physiological factors and may improve diagnostics, be an important tool for cardiac rehabilitation and for health professionals examining patient's health risks in the future.

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Appendice

Appendix A
Borg Scale

Table 8. Borg Scale, an subjective rating of perceived exertion (6-20) (27).

6	
7	Very, very light
8	
9	Very light
10	
11	Fairly light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Very, very hard
20	

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