Muscle changes due to exercise in COPD and healthy individuals

Submission date	Recruitment status No longer recruiting	[X] Prospectively registered		
25/04/2013		☐ Protocol		
Registration date	Overall study status	Statistical analysis plan		
26/04/2013	Completed	[X] Results		
Last Edited	Condition category	Individual participant data		
06/03/2018	Respiratory			

Plain English summary of protocol

Background and study aims

Chronic obstructive pulmonary disease (COPD) is predominantly a lung disease that is irreversible. Interestingly we have found that patients with this condition are not only short of breath, but also struggle with activities of daily living (walking, housework, climbing stairs etc) that seems not to be related to the lung damage. This has been an area of growing interest. We have found that in COPD patients, muscle functions (mostly in the legs) are abnormal when compared to healthy individuals. This is a possible target of treatment, both in terms of providing focused exercise and also possible drug treatment.

Who can participate?

COPD patients aged 60-80 and healthy sedentary people (not doing more than 30 minutes of exercise three times a day) aged 18-35 or 60-80.

What does the study involve?

The study involves 8 weeks of training; 3 times a week of cycling. This is then followed by 4 weeks of de-training where there is no exercise. Patients have five muscle biopsies at different time points of the study, where we perform numerous muscle function tests. We also assess their exercise capacity, muscle strength and mass at 4-5 time points throughout the study.

What are the possible benefits and risks of participating?

We would expect you to benefit from improvements in your fitness as a result of the exercise programme, although this may not occur in all participants. We hope the information we get from this study will be helpful in understanding the problem of muscle dysfunction in patients with COPD and help develop treatments for this problem. The risks are minimal. The muscle biopsies are low risk and will be done by an experienced clinician under local anaesthetic, and people can carry on with normal activities straight away with minimal discomfort. You may be left with a small scar at the end.

Where is the study run from?

The study will be involved at the Leicester Glenfield Hospital and Nottingham University, at the Queens Medical Centre. We shall be recruiting from Nottingham and Leicester.

When is the study starting and how long is it expected to run for? May 2013 to January 2015

Who is funding the study? Medical Research Council (UK)

Who is the main contact? Prof Michael Steiner michael.steiner@uhl-tr.nhs.uk

Contact information

Type(s)

Scientific

Contact name

Prof Michael Steiner

Contact details

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Additional identifiers

Protocol serial number 14080

Study information

Scientific Title

Mitochondrial adaptations to Aerobic Training in chronic obstructive pulmonary disease and Health: the MATCH study

Acronym

MATCH

Study objectives

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of illness and disability. Patients are breathless and have limited exercise capacity.

Interventions targeting the skeletal muscles may be of therapeutic benefit, as demonstrated by the unequivocal benefits of exercise training in the context of pulmonary rehabilitation.

The mitochondria perform a vital function for oxidative energy metabolism within cells. They are responsible for the aerobic energy production in muscle cells which is essential for prolonged exercise. A major contributor to the exercise limitation experienced by COPD patients is recognised to be a reduction in oxidative capacity at the level of the skeletal muscle mediated by reduced mitochondrial density and function.

Mitochondrial density and function are potential therapeutic targets in COPD, however it remains uncertain whether impaired mitochondrial density and/or function are attributable to ageing, inactivity and deconditioning, a COPD specific mitochondropathy or a combination of these factors. This study will assess:

- 1. Mitochondrial quality, density and function in COPD patients compared to both age-matched, and young healthy control (HC) volunteers.
- 2. The impact of aerobic (endurance) training on whole-body oxygen consumption, muscle gene expression and mitochondrial density and function in COPD patients and young and old healthy controls and the time-course of any changes observed.
- 3. The impact of detraining on these same parameters following exercise training. This is an important facet of the study as it is known that in healthy, young volunteers the decline in mitochondrial function with detraining is more rapid than the decline in maximal oxygen consumption. It is pertinent therefore to know whether this is exacerbated in COPD particularly given they are likely to be more inactive during detraining.

Importantly the approach proposed will enable us to differentiate the effect of ageing from any COPD specific effects.

More details can be found at: http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=14080

Ethics approval required

Old ethics approval format

Ethics approval(s)

NRES Committee West Midlands - Coventry & Warwickshire, ref number: 13/WM/0075

Study design

Non-randomised interventional and observational case-controlled study

Primary study design

Interventional

Study type(s)

Quality of life

Health condition(s) or problem(s) studied

Chronic obstructive pulmonary disease

Interventions

The study involves 8 weeks of aerobic exercise training: cycling 3 times per week. This is then followed by 4 weeks of de-training where there is no exercise. Patients have five muscle biopsies at different time points of the study, where we perform numerous muscle function tests. We also assess their exercise capacity, muscle strength and mass at 4-5 time points throughout the study.

Intervention Type

Other

Phase

Not Applicable

Primary outcome(s)

Primary end points for outcome will be measured at baseline, 1 week post baseline, 4 weeks post exercise, 8 weeks post exercise (end of exercise), and post detraining (4 weeks) for muscle biopsies.

- 1. These will be the tests we shall be measuring from the biopsies: mitochondrial DNA and deletions to provide a measure of mitochondrial quality (baseline biopsy only).
- 2. Maximal rates of mitochondrial ATP production (using a variety of mitochondrial substrates) utilising a high-sensitivity firefly-luciferase method for determining mitochondrial ATP production capacity that is known to be highly sensitive to defects in mitochondrial function in human endotoxaemia and improvements in mitochondrial function with exercise training.
- 3. Mitochondrial enzyme maximal activities (pyruvate dehydrogenase complex, TCA cycle and electron transport chain) to give an index of mitochondrial density. In addition, cytosolic enzyme activities will be determined to assess relative changes in non-mitochondrial energy production capacity.
- 4. We will conduct a broad investigation of muscle mRNA expression using low density array (LDA) cards. Specifically, we will utilise automated 384 well cards to assess targeted gene expression covering a wide range of gene families associated with inflammation, apoptosis, cell cycle/growth/differentiation, mitochondria, RNA processing, DNA replication and repair, immune responses, the NFkB pathway, the ubiquitin proteasome pathway and other metabolic processes.
- 5. Guided by the outcome of the gene expression measurements, targeted proteins will also be measured by Western blotting (including mitochondrial linked targets e.g., PPARs, PGC1α, AMPK).
- 6. Muscle fibre composition using silver staining (to control for training induced increases in slow muscle fibre area).

Key secondary outcome(s))

- 1. Muscle strength testing
- 2. Maximal VO2
- 3. Body composition (fat free mass)

Completion date

01/01/2015

Eligibility

Key inclusion criteria

Current inclusion criteria as of 26/02/2016:

COPD subjects:

- 1. Clinically stable patients (no exacerbation within last 4 weeks)
- 2. Aged 60-80
- 3. Spirometric criteria for COPD (FEV1/FVC < 0.7, FEV1 < 80% predicted) with significant exercise limitation (MRC breathlessness score 3 or worse)
- 4. Clinical picture of COPD

Healthy control subjects:

- 1. Age matched (60 80 years) and young (18 35 years) healthy controls will be recruited from the local population
- 2. Spirometric criteria (FEV1/FVC >0.7, FEV1 >80%)

Previous inclusion criteria:

COPD subjects:

- 1. Clinically stable patients (no exacerbation within last 4 weeks)
- 2. Aged 60-80
- 3. Spirometric criteria for COPD (FEV1/FVC < 0.7, FEV1 < 80% predicted) with significant exercise limitation (MRC breathlessness score 3 or worse)
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Healthy control subjects:

- 1. Age matched (60 80 years) and young (18 30 years) healthy controls will be recruited from the local population
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Participant type(s)

Mixed

Healthy volunteers allowed

No

Age group

Senior

Sex

Αll

Key exclusion criteria

COPD subjects:

- 1. Subject on any of the following:
- 1.1. Long-term oral corticosteroids
- 1.2. Anticoagulation (e.g. warfarin)
- 1.3. Long term oxygen therapy
- 2. Co-morbid conditions preventing exercise training or causing exercise limitation or intramuscular inflammation including type II diabetes.
- 3. Undergone pulmonary rehabilitation in the preceding year (as there may be residual benefits)
- 4. Current smokers will be excluded as cigarette smoke may have a direct affect on mitochondrial function independent of disease state. To exclude the possibility of residual effects of smoking, all participants must report no smoking habit for 1 year prior to entry into the study

Healthy control subjects:

- 1. Any inflammatory illnesses (e.g. type II diabetes, inflammatory bowel disease)
- 2. Any condition causing exercise limitation
- 3. Engaged in regular physical activity or exercise regime
- 4. As for COPD patients, healthy volunteers must not have smoked in the 1 year preceding entry into the study

Date of first enrolment

07/05/2013

Date of final enrolment

01/01/2015

Locations

Countries of recruitment

United Kingdom

England

Study participating centre Glenfield Hospital

Leicester United Kingdom LE3 9QP

Sponsor information

Organisation

University Hospitals of Leicester NHS Trust (UK)

ROR

https://ror.org/02fha3693

Funder(s)

Funder type

Research council

Funder Name

Medical Research Council (MRC) (UK) Grant Codes: G1001362/1

Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Funder Name

NIHR Leicester Respiratory Biomedical Research Unit (UK)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2014		Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes