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The effect of exercise and the immune system on muscle wasting in chronic kidney disease

Submission date
30/10/2017

Recruitment status
No longer recruiting

Registration date
07/11/2017

Overall study status
Completed

Last Edited
26/04/2021

Condition category
Urological and Genital Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Chronic kidney disease (CKD) is a disease that causes the kidneys to stop working as well over time. People with CKD often experience problems with their muscles such as weakness and soreness which can make daily activities, like walking and climbing stairs, more difficult. Our previous research has discovered some reasons why this happens, but we still do not fully understand it. One reason may involve the immune system, which is important in repairing and regenerating our muscles after exercise, but not many studies have investigated the effect of exercise on the muscle of people with CKD. This research is important as we need to find ways to help prevent muscle problems in people with kidney disease. Exercise is an important part of a healthy lifestyle and is increasingly recognized as an important aspect in the treatment of CKD. Resistance exercise is particularly relevant to improving muscle size and strength. However, the response of muscles in people with CKD may be different from the general population. This may result in less benefits, possibly contributing to smaller, weaker muscles. An improved understanding of the response of muscles in CKD patients to exercise will hopefully lead to improved methods of preventing loss of muscle mass and strength, directly improving outcomes for patients. The aim of this study is to investigate the response of muscles in response to exercise.

Who can participate?
Adults aged 18 and older who either have CKD or are healthy.

What does the study involve?
This study has two parts. In the first parts, participants with CKD complete a survey about their experiences of muscle problems and how this affects their day to day life. In the second part, participants with CKD and healthy controls are asked to perform a single exercise session. Exercise will involve resistance exercises of the legs. Participants provide blood and saliva samples as well as small piece of muscle tissue taken before and after the exercise (at four and 48 hours after). Participants are compared to assess the effect on a resistance exercise session on the muscle of CKD patients to healthy individuals.

What are the possible benefits and risks of participating?
Benefits to participating include contributing to research that will improve treatment outcomes

for CKD patients, receiving an accurate assessment of strength and a supervised resistance exercise session. Risks of participating are minimal. There is a small risk of muscular injury when exercising, however exercise difficulty will be specific to the individual and participants will not be asked to exercise beyond the point they feel comfortable with. Exercise will also be performed after a warm-up. There is also a small risk of discomfort and infection when performing a muscle biopsy. However, this procedure will be performed under local anaesthetic and in a sterile environment by a trained doctor.

Where is the study run from?
Leicester General Hospital (UK)

When is the study starting and how long is it expected to run for?
October 2017 to December 2018

Who is funding the study?
Kidney Research UK (UK)

Who is the main contact?
Professor Alice Smith
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Contact information

Type(s)
Scientific

Contact name
Prof Alice Smith

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
35952

Study information

Scientific Title
Intramuscular and Inflammatory Response to Acute Exercise in Chronic Disease (I-RACE)

Acronym
I-RACE

Study objectives
This study aims to investigate the mechanisms of skeletal muscle wasting in patients with chronic kidney disease (CKD) and the intramuscular response to acute exercise.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East Midlands - Derby Research Ethics Committee, 21/10/2017, ref: 17/EM/0357

Study design
Non-randomised; Both; Design type: Treatment, Prevention, Education or Self-Management, Cellular, Psychological & Behavioural, Complex Intervention, Physical, Rehabilitation, Cross-sectional

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Chronic kidney disease

Interventions
This study has 2 separate parts A and B. Part A is a survey. Part B is a single-centre observational /exploratory study involving up to 4 visits over approximately two weeks.

Part A:
Participants with CKD are provided with a survey pack containing four questions to assess:
1. Muscle Wasting
2. Physical Activity
3. Physical Function
4. Symptom Perception

Part B:
Participants and healthy controls undergo a single bout of resistance exercise with measurements before and at two points after, approximately four and 48-hours after. Resistance exercise consists of leg press and leg extension exercise.Blood, saliva and muscle tissue are taken at each measurement point.

Intervention Type
Other

Primary outcome measure
Immune cell populations and phenotype, inflammation, anabolic and catabolic processes, myogenesis and expression of proteins important in the maintenance of muscle mass using flow cytometry, PCR, western blotting and immuno-fluorescent staining is measured using the muscle biopsy samples at baseline, 4 hours post and 48 hours post exercise.

Secondary outcome measures
1. Metabolic and immune function is measured using blood samples at baseline, 4 hours post and 48 hours post exercise
2. Inflammation is measured using blood samples at baseline, 4 hours post and 48 hours post exercise
3. Proteins related to the maintenance of muscle mass are measured using blood samples at baseline, 4 hours post and 48 hours post exercise
4. Oxidative stress is measured using blood samples at baseline, 4 hours post and 48 hours post exercise
5. Immune function is measured using saliva at baseline, 4 hours post and 48 hours post exercise
6. Relationships between muscle wasting, levels of physical activity, physical function and symptoms perceptions are measured using questionnaire responses at baseline, 4 hours post and 48 hours post exercise

Overall study start date
04/09/2017

Completion date
03/09/2022

Eligibility

Key inclusion criteria
Patient inclusion criteria:
Diagnosed CKD patients (eGFR<60ml/min/1.73m2). Renal transplant recipients (RTRs) will also be eligible.

Healthy control inclusion criteria:
Individuals with not diagnosed kidney disease (eGFR>80ml/min/1.73m2).

All participants must be willing and able to give informed consent for participation in the study.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 65; UK Sample Size: 65

Key exclusion criteria
Patient exclusion criteria:
1. Age <18 years
2. Female participants who are pregnant, lactating, or planning pregnancy during the course of the study
3. Scheduled elective surgery or other procedures requiring general anaesthesia during the study
4. Any other significant disease or disorder (i.e. significant co-morbidity including unstable hypertension, potentially lethal arrhythmia, myocardial infarction within 6 months, unstable angina, active liver disease, uncontrolled diabetes mellitus (HbA1c ≥9%), advanced cerebral or peripheral vascular disease) which, in the opinion of the patient's own clinician, may either put the participants at risk because of participation in the study, or may influence the result of the study, or the participant's ability to participate in the study
5. Inability to give informed consent or comply with testing and training protocol for any reason
6. Individuals who are currently, or have in the past 6 months, used immunosuppressive or anti-inflammatory medication other than that required by renal transplant recipients (RTRs) to prevent graft rejection

Healthy control exclusion criteria:
1. Age <18 years
2. Female participants who are pregnant, lactating, or planning pregnancy during the course of the study
3. Scheduled elective surgery or other procedures requiring general anaesthesia during the study
4. Chronic Kidney Disease (eGFR<80mL/min/1.73m2)
5. Any other significant disease or disorder (i.e. significant co-morbidity including unstable hypertension, potentially lethal arrhythmia, myocardial infarction within 6 months, unstable angina, active liver disease, uncontrolled diabetes mellitus (HbA1c ≥9%), advanced cerebral or peripheral vascular disease)
6. Individuals who are currently, or have in the past 6 months, used immunosuppressive medication
7. Inability to give informed consent for any reason

Date of first enrolment
08/11/2017

Date of final enrolment
02/09/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Leicester General Hospital
Gwendolen Road
Leicester
United Kingdom
LE5 4PW

Sponsor information

Organisation
University Hospitals of Leicester NHS Trust

Sponsor details
Gwendolen House
Gwendolen Road
Leicester
Leicester
England
United Kingdom
LE5 4QF

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/02fha3693

Funder(s)

Funder type
Charity

Funder Name
Kidney Research UK (KRUK)

Results and Publications

Publication and dissemination plan

The results of this study will be presented in abstract form at relevant scientific and medical conferences, and will be published in appropriate peer-reviewed journals. The Chief Investigator as custodian of the data will oversee preparation and submission of abstracts and journal articles, and her permission must be obtained prior to preparation of any reports including reference to the study, data or results. Authorship will include all individuals who have made significant contributions to study design and execution, data analysis and interpretation and manuscript preparation. Authors and order will be at the discretion of the Chief Investigator. Individuals who have had involvement in the study but made insufficient intellectual contribution for authorship will be acknowledged in manuscripts. All authors will be given ample opportunity to review and approve all abstracts and manuscripts before submission, and those acknowledged will be asked for approval of their inclusion before publication.

Intention to publish date

03/09/2023

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	observational results	22/04/2021	26/04/2021	Yes	No
HRA research summary			28/06/2023	No	No