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Steroid hormone metabolism and muscle loss in chronic kidney disease

Submission date	Recruitment status	[_] Prospectively registered
24/02/2022	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
11/04/2022	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
19/05/2022	Urological and Genital Diseases	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
People with chronic kidney disease (CKD) develop muscle loss as a complication of their disease. Not only do they experience weakness and fatigue as a result, but they are also at greater risk of injury from falls, admissions to hospital, needing care and early death. We do not fully understand what causes muscle loss in kidney disease. This has made it difficult to develop treatments and other ways to help people with this problem.

In kidney disease, muscles do not respond normally to exercise to maintain their size, strength and function. We know that kidney disease causes problems with the way in which our cells generate energy through the process of metabolism. Specifically, it means that the muscles generate energy less efficiently, and thus are not able to maintain muscle mass and strength. Previous research suggests that excessive signalling of the hormone cortisol plays an important role in this disease process. The aim of our study is to learn about hormone changes that occur in chronic kidney disease and their role for muscle loss. The findings from this study will help us to understand why patients with kidney disease experience muscle loss and guide the development of new treatments for these patients.

Who can participate?
The study will invite 60 - 80 year old adults with chronic kidney disease and healthy volunteers to participate.

What does the study involve?
Participation will involve a single research visit for sharing information on health and lifestyle, testing muscle function, and donating blood, urine, and muscle tissue samples. Samples will then be tested in the laboratory to study how metabolism changes in kidney disease.

What are the possible benefits and risks of participating?
Travel expenses related to study participation will be reimbursed and participants will receive a light meal during the study visit.
Collecting the blood sample can leave a small bruise for a few days. There is an extremely low risk of infection or bleeding from the muscle biopsy and of an allergic reaction to local anaesthetic. Pain and numbness has been reported once in many thousands of otherwise

uncomplicated biopsies. Participants may notice a small scar at the site of the biopsy, but scars should improve within 6-12 months after the biopsy.

Where is the study run from?
University Hospital Birmingham and the University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
February 2022 to August 2025

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

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
288991

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 288991, CPMS 52504

Study information

Scientific Title
The role of cortisol and steroid hormone metabolism for sarcopenia in chronic kidney disease; a cross-sectional study

Acronym
SMK study

Study objectives
Our study will address how shifts in steroid hormone metabolism in humans with CKD affect skeletal muscle. Our hypothesis proposes that elevated glucocorticoid activation in skeletal muscle tissue contributes to muscle protein loss in patients with CKD.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Single-centre observational cross-sectional study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Aetiology of sarcopenia in patients with chronic kidney disease

Interventions

Participation will involve a single research visit for sharing information on health and lifestyle, testing muscle function, and donating blood, urine, and muscle tissue samples. Samples will then be tested in the laboratory to study how metabolism changes in kidney disease.

Data collection procedures:
a) Person characteristics and medical history
b) Short Nutrition Assessment Questionnaire
c) International Physical Activity Questionnaire – short form
d) Body-mass-index
e) Body composition by bioelectrical impedance assessment
f) Hand grip strength
g) Short Physical Performance Battery

Sample collection procedures:
a) Blood sample (for profiling of biochemical, metabolic, endocrine and inflammatory markers)
b) Quadriceps muscle biopsy (for ex vivo metabolic steroid activation assays, markers of anabolic /catabolic balance, histology and primary cell culture experiments)
c) 24-hour urine sample (for urinary steroid profile and creatinine clearance)

Intervention Type
Other

Primary outcome(s)
Conversion rate of cortisone to cortisol measured in skeletal muscle biopsies ex vivo at baseline using a radiolabelled tracer assay.

Key secondary outcome(s))
1. Urinary steroid metabolome measured using liquid-chromatography/mass-spectrometry at baseline
2. Handgrip strength measured using a handheld dynamometer at baseline
3. Body composition measured using bioelectrical impedance analysis at baseline
4. Physical function measured using the Short Physical Performance Battery test at baseline
5. Malnutrition measured using the Short Nutrition Assessment Questionnaire at baseline
6. Physical activity measured using the International Physical Activity Questionnaire (short form) at baseline)
7. Serum cytokine and hormone levels measured by ELISA and LUMINEX assays at baseline
8. Expression of anabolic and catabolic markers in skeletal muscle biopsies using qPCR and Western blot analysis at baseline

Completion date
01/08/2025

Eligibility

Key inclusion criteria
1. Men and women
2. Age 60-80 years
3. For CKD group (recruitment target 30): chronic kidney disease stage IV or V (eGFR less than 30ml/min for more than 3 months)

4. For control group (recruitment target 20): no history of kidney disease or other major chronic illness
5. Willing and able to provide informed consent

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Receive steroid medications or hormone replacement therapy other than thyroxine for well-controlled hypothyroidism
2. Have a primary neurological or muscle disease that impairs muscle function
3. Be at extremes of body weight (BMI <18 or >35kg/m²)
4. Have a diagnosis of cancer in the past 5 years (except non-melanoma skin cancer)
5. Suffered an acute illness requiring hospital admission within the past month
6. Have a bleeding predisposition or receive anticoagulation (except aspirin that can be suspended for 3 days without significant clinical risk)
7. Be enrolled in another clinical trial with a treatment intervention within past four months

Date of first enrolment
01/04/2022

Date of final enrolment
01/04/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Queen Elizabeth Hospital
University Hospitals Birmingham NHS Foundation Trust
Mindelsohn Way
Edgbaston
Birmingham
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B15 2GW

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date