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The effect of exercise and nutritional supplementation on frailty and dialysis-related measures in end-stage kidney disease patients- A pilot study

Submission date
23/01/2024

Recruitment status
No longer recruiting

Registration date
26/01/2024

Overall study status
Completed

Last Edited
21/10/2024

Condition category
Urological and Genital Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
"Frailty" is a medical term for a condition that affects a large number of people as they get older. In many ways, it refers to what people mean when they say someone is "getting old", however, it is a condition that can affect people of all ages. One of the main ways to identify frailty is to look for evidence of weight loss, weakness, slowness, reduced activity or a feeling of exhaustion. Another is to count up the number of illnesses or impairments someone has accumulated over their life. Frailty is common and becoming even more so. Overall, about 1 in 10 people are frail. This increases as we age, rising to almost 1 in 4 over the age of 90. It is also very common for patients on dialysis with approximately 3 in 10 people on dialysis being frail. Frailty means that an individual is less well able to tolerate anything that may affect their well-being (for example, infection, side-effects of medications, hospital admission or medical procedures). It is known that unfortunately, the more frail a person is, the more likely they are to develop a range of illnesses, be admitted to hospital or require nursing home care. Thankfully, more and more research shows that exercise and nutritional supplements can slow the onset of frailty. Some research has also demonstrated the benefits of 'reversing frailty' in the general population with exercise and nutrition. However, very few studies have included patients who are on dialysis. This research study is taking place to find out if the benefits of exercise and nutrition also apply to frail individuals with kidney disease who are receiving dialysis and whether this intervention can reverse frailty in this population.

Who can participate?
Frail adults with end-stage kidney disease aged 18 years old and over will be identified from the dialysis population at University Hospital Waterford.

What does the study involve?
Once identified patients will be randomized to an intervention arm and will undergo a 12-week exercise program or a control arm and will continue with their usual care and not undergo the exercise intervention. Patients will have their daily protein intake assessed. Patients allotted to

the intervention arm will also be advised to supplement their diet with an extra protein supplement to achieve a daily protein intake of 1.2g/kg/day. The protein supplement will be individualized for each patient and will be chosen in conjunction with the Renal Dietician based in the dialysis unit.

What are the possible benefits and risks of participating?
There are no guarantees that this intervention will be of benefit. The available evidence would suggest that exercise and nutritional supplementation can improve physical function and psychological wellbeing in frail adults in the general population. However, this has not been conclusively shown in frail adults with kidney disease on dialysis and that is what this study is helping to answer.

Engaging in exercise brings an associated risk of minor complications such as muscle aches or strain. If people have a history of (or several risk factors for) heart disease or lung disease, there may also be a risk of more serious adverse effects. It is difficult to put an exact figure on this risk as it differs from person to person. To limit this risk, a set of screening questions are asked and advice is given about how to know when a participant might be exercising too vigorously. For emergencies, the hospital staff will be able to attend to the participant like for all patients on dialysis.

Where is the study run from?
University Hospital Waterford (Ireland)

When is the study starting and how long is it expected to run for?
February 2023 to November2024

Who is funding the study?
Royal College of Surgeons in Ireland (RCSI) under the Strategic Academic Recruitment (StAR) program.

Who is the main contact?
Robert Casey, 110309713@umail.ucc.ie. This research study will be primarily organized by Dr. Robert Casey over two years from July 2023 to July 2025, to achieve the academic qualification of MD as part of his specialist training in Nephrology. The study will be supervised by Dr. Catherine Brown (Consultant Nephrologist), Dr Sean Leavey (Consultant Nephrologist) and Dr. Padraig Bambrick (Consultant for Medicine for the Elderly).

Contact information

Type(s)
Public, Scientific

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Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
The effect of exercise and nutritional supplementation on frailty and dialysis-related measures in end-stage kidney disease patients- A pilot study

Study objectives
Current hypothesis as of 21/10/2024:

The hypothesis is that a standardized exercise programme for frail adults with end-stage kidney disease is feasible to perform.

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Previous hypothesis:

The hypothesis is that a standardized exercise programme for frail adults with end-stage kidney disease will lead to a measurable difference in clinical markers of frailty

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 18/09/2023, The Research Ethics Committee, REC, HSE, South East (Research Ethics Office, University Hospital Waterford, Waterford, X91 ER8E, Ireland; +351 051 842391; Martina.Walsh5@hse.ie), ref: 23.49

2. Approved 15/10/2024, The Research Ethics Committee, REC, HSE, South East (Research Ethics Office, University Hospital Waterford, Waterford, X91 ER8E, Ireland; +351 051 842391; Martina.Walsh5@hse.ie), ref: 24.36

Study design
Single-center interventional pilot randomized controlled trial

Primary study design
Interventional

Secondary study design
Pilot randomized controlled trial

Study setting(s)
Hospital

Study type(s)
Other, Quality of life, Treatment

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Frailty and end-stage kidney disease

Interventions
Current interventions as of 21/10/2024:

This study will take the form of a non-blinded pilot randomized controlled trial. Frail adults with end-stage kidney disease (ESKD) will be identified from the ESKD patient population in University Hospital Waterford. Frail patients will be identified using the Rockwood frailty scale. Once identified patients will be randomized using a stratified randomization method to aid balance for covariates of age and sex to an intervention arm and will undergo either a 12-week exercise program or a control arm and will continue with usual care. Patients will have their daily protein intake assessed. Patients randomized to the intervention arm will also be advised to supplement their diet with extra protein to achieve a daily protein intake of 1.2g/kg/day. The protein supplement will be individualized for each patient and will be chosen in conjunction with the Renal Dietician based in the dialysis unit.

All patients included in the study will undergo baseline assessment and repeat assessment at 12 weeks and 18 weeks. Assessments will take place in the hemodialysis unit at University Hospital Waterford.

The study will develop a novel exercise program suitable for frail adults with ESKD. To do so, a consensus group will be formed comprising of Consultant Nephrologists, a Consultant Geriatrician, a Nephrology Registrar, senior physiotherapists, a senior occupational therapist, senior dialysis nurses and a Sports & Exercise Scientist. A range of exercises will be agreed upon via an appropriate group consensus technique, in the areas of aerobic, resistance, balance and flexibility training.

To assess feasibility outcomes such as acceptability, demand, implementation, practicality, integration, adaptation, and expansion we will perform short semi structured interviews with study participants once the intervention is complete. We will also organize a focus group with dialysis staff nurses. Both the interviews and the focus group will be conducted in a quiet private area. The interviews will be relatively short - aiming for 20-30 minutes each. Adherence data to the exercise intervention and protein supplementation was also collected over the intervention period.

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There will be an initial one-month pilot involving a small number of participants to develop the exercise program. This period will be used to assess the appropriateness, tolerability and preference of the subjects for various exercises, as well as the optimal duration, intensity, rate of escalation and duration of sessions. There will then be refinement of the protocol through further rounds of the group consensus process.

Intervention Type

Mixed

Primary outcome measure
Current primary outcome measure as of 21/10/2024:

1. Evaluate the feasibility of conducting a definitive randomized controlled trial. Acceptability, demand, implementation, practicality, integration, adaptation, and expansion measured post completion of the exercise intervention using:
1.1.Semi-structured interviews with ESKD participants in the study
1.2.Focus group with nursing staff from the dialysis unit
2. Change in frailty score measured using the Fried Frailty Scale at baseline, 12 and 18 weeks

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Previous primary outcome measure:

Change in frailty score measured using the Fried Frailty Scale at baseline, 12 and 18 weeks

Secondary outcome measures
The following secondary outcome measures are assessed at baseline,12 weeks,18 weeks:
1. Change in frailty-related biomarkers/inflammatory markers measured using blood C-reactive protein (CRP) and D-Dimer levels
2. Change in dialysis adequacy measured using urea reduction ratio (URR)/Kt/V
3. Change in QoL scores measured using the Montreal Cognitive Assessment (MoCA), The Kidney Disease Quality of Life-Short Form and the Beck Depression Inventory-II
4. Number of treatment-related adverse outcomes – non-serious adverse events (i.e fatigue, pain) collected weekly by participant review; serious adverse events (i.e hospitalization, serious risk of deterioration in patient health, death) collection on occurrence and review event with principal investigator to determine if likely related to intervention

Overall study start date
01/02/2023

Completion date
15/11/2024

Eligibility

Key inclusion criteria
1. Adults >18 years old
2. Patient with ESKD currently receiving haemodialysis or peritoneal dialysis
3. Identified as pre-frail/frail using Freid Frailty Scale

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
25

Key exclusion criteria
1. Severe functional disability
2. Cognitive impairment likely to preclude involvement in an exercise program
3. Current participation in an alternative exercise programme
4. Poorly controlled angina or heart failure or coronary event in the last 6 months
5. Receiving palliative care or life expectancy less than 6 months

Date of first enrolment
01/02/2024

Date of final enrolment
01/04/2024

Locations

Countries of recruitment
Ireland

Study participating centre
University Hospital Waterford
Dunmore Road
Waterford
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X91 ER8E

Sponsor information

Organisation
University Hospital Waterford

Sponsor details
Dunmore Road
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Sponsor type
Hospital/treatment centre

Website
https://www.hse.ie/eng/services/list/3/acutehospitals/hospitals/waterford/

ROR
https://ror.org/007pvy114

Funder(s)

Funder type
University/education

Funder Name
Royal College of Surgeons in Ireland

Alternative Name(s)
Coláiste Ríoga na Máinleá in Éirinn, RCSI

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Ireland

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
01/08/2025

Individual participant data (IPD) sharing plan
The data sets generated during and/or analysed during the current study will be available upon request from Robert Casey, 110309713@umail.ucc.ie.
1. The type of data that will be shared - The information recorded as part of this study will remain confidential between the participant and the researcher. No paper records will contain personal identifiers. Instead, they will be marked with a code which requires a key, held only by the researcher. These paper records will be securely stored in a locked filing cabinet and then transferred to an electronic record where they will be encrypted at point of storage on local

secure storage and only the Principal Investigator (Dr Catherine brown) and MD student (Dr Robert Casey) will have a decryption key. It may be necessary to share this data with researchers within the RCSI research network for assistance with statistical analysis. If this was required, the data would be irreversibly anonymised prior to transfer to other researchers. All data subjects have the right to request access to their data and a copy of it.
2. Timing for availability - All data subjects have the right to request access to their data and a copy of it. Would be made available upon request.
3. Whether consent from participants was required and obtained - Consent will be obtained by Dr. Robert Casey, MD student. Every effort will be made to ensure that all participants are fully informed prior to enrolment, through provision of all information in suitably worded language and visual representations to maximise understanding. In addition, an opportunity will be provided for participants to seek clarification of any issues prior to agreeing to participate. If queries or concerns remain after this process, then the individual may request assistance from a specified relative/friend/carer to assist them in gaining understanding to their satisfaction and achieve informed consent through an assisted decision-making process.
4. Comments on data anonymization- Data collected will be coded at point of collection and paper records securely stored in a locked filing cabinet in the dialysis unit. The data collected will be encrypted at point of storage on local secure storage-only the PI and MD student will have a decryption key. It may be necessary to share this data with researchers within the RCSI research network for assistance with statistical analysis. If this was required, the data would be irreversibly anonymised prior to transfer to other researchers.
5. Any ethical or legal restrictions – no ethical or legal restrictions

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			24/01/2024	No	Yes
Participant information sheet			24/01/2024	No	Yes