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Accuracy of glomerular filtration rate (GFR) estimation using creatinine and cystatin C and albuminuria for monitoring disease progression in patients with stage 3 chronic kidney disease: the eGFR-C study

Submission date
26/09/2013

Recruitment status
No longer recruiting

Registration date
08/10/2013

Overall study status
Completed

Last Edited
29/07/2024

Condition category
Urological and Genital Diseases

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

Plain English summary of protocol
http://www.birmingham.ac.uk/research/activity/mds/trials/bctu/trials/renal/egfr-c/participants/index.aspx

Study website
http://www.birmingham.ac.uk/egfr-c

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT02433002

Secondary identifying numbers
HTA 11/103/01, UKCRN ID 15268

Study information

Scientific Title
Accuracy of glomerular filtration rate (GFR) estimation using creatinine and cystatin C and albuminuria for monitoring disease progression in patients with stage 3 chronic kidney disease - prospective longitudinal study in a multi-ethnic population: the eGFR-C study

Acronym
eGFR-C

Study objectives
The eGFR-C study will assess the accuracy of current and alternative tests of kidney function against a reference test in people with moderate (stage 3) chronic kidney disease (CKD).

More details can be found at: http://public.ukcrn.org.uk/Search/StudyDetail.aspx?StudyID=15268
More details can be found at: http://www.nets.nihr.ac.uk/projects/hta/1110301
Protocol can be found at: https://www.birmingham.ac.uk/egfrc/documents (version 4.0 02.02.17)

Ethics approval required
Old ethics approval format

Ethics approval(s)
South East Coast Surrey REC, 09/10/2013, ref 13/LO/1349

Study design
Observational prospective longitudinal cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet

Patient information can be found at http://www.birmingham.ac.uk/research/activity/mds/trials/bctu/trials/renal/egfr-c/participants/sheet.aspx

Health condition(s) or problem(s) studied
Topic: Renal and Urogenital; Subtopic: Renal and Urogenital (all Subtopics); Disease: Renal

Interventions
Main study: 1300 patients. Biological variability study: In a sub-study 20 participants will undergo the reference test four times over four weeks and then exit the study.

Iohexol GFR tests, 1300 participants will undergo baseline (month 0) and final (month 36) reference GFR, estimated GFR (eGFR) and urinary albumin-to-creatinine ratio (ACR) tests. Additionally they will provide ACR and eGFR tests at 6-monthly intervals. A subset of the cohort (n=375) will receive annual reference GFR tests.

Participants will be recruited from hospital clinics and GP practices at six major UK centres.

Participants will undergo reference GFR testing at study entry with a second follow-up reference test three years later. The reference test involves injecting a small amount of iohexol into a vein and taking blood samples over the next 4 hours to see how quickly the iohexol disappears from the blood stream as a result of glomerular filtration. The rate at which iohexol disappears is equivalent to the level of kidney function. Blood tests for monitoring kidney function, including testing for creatinine and cystatin C, and measurement of urinary albumin will be done every six months during the study period. Iohexol measured GFR will be accepted as the reference (gold standard) measure of kidney function against which each GFR-estimating equations will be compared. The alternative estimated measures of GFR, derived from measuring substances (creatinine and cystatin C) in the blood, will be compared against the reference test. An important outcome is how much the reference test changes over the three years of the study, and how well the surrogate measures reflect this change. We will also collect accurate test cost data for subsequent cost-effectiveness analysis (e.g. do the relative costs of the tests justify any change in practice due to improved performance of one test compared to another?).

Follow-up length: 36 months

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. To estimate and compare the accuracy and precision of GFR-estimating equations based on the Modification of Diet in Renal Disease (MDRD) equation and three Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations using either creatinine or cystatin C or a combination of both in people with stage 3 CKD.
2. To estimate the accuracy and precision of the GFR-estimating equations according to ethnic group (particularly Caucasians, African-Caribbean and South-Asian), and baseline diabetes and proteinuria.
Percentage error in eGFR compared to reference GFR. Values will be computed (primary outcome measures 1 and 2) using baseline data for each of the four eGFR equations, and the proportions within 30% (P30) of the reference standard quoted and compared as a measure of

accuracy and precision.
3. To evaluate and compare how accurately these GFR-estimating equations reflect change in GFR over three years. Difference in rate of change in eGFR compared to rate of change in reference GFR. Rates of change will be estimated using linear regression and the change per annum and percentage change per annum compared to baseline values will be computed. Large error will be defined as differing by more than 3 mL/min/1.73 m^2/year or by 5 percent points per annum.

Secondary outcome measures
1. To establish which GFR-estimating equation, together with ACR, or ACR alone, most accurately predicts those people that have progressive loss of kidney function (CKD progression). Progressive loss of kidney function defined as decline in GFR of more than 10 mL /min/1.73 m^2/3 years or increase in albuminuria category as defined by Kidney Disease: Improving Global Outcomes (KDIGO).
2. To compare the effectiveness and costs of monitoring strategies for identifying people that have progressive loss of kidney function (CKD progression) utilising different GFR-estimating equations and test schedules, accounting for differences in risk of progression. Measured using Cost per quality-adjusted life-year (QALY).

Sub-study of patterns of disease progression
To estimate and model disease progression (decline in GFR or increase in ACR) according to ethnic group (particularly Caucasians, African-Caribbean and South-Asian), and baseline diabetes and proteinuria. Difference in rate of change in eGFR compared to rate of change in reference GFR based on measurements made every 12 months.

Additional study of intra-individual biological variation
Within-individual (CVI) variation and the critical difference (reference change value, RCV) for reference GFR and the estimated GFR equations.

Overall study start date
01/02/2014

Completion date
30/06/2020

Eligibility

Key inclusion criteria
1. Male and female, aged 18 years or over
2. Patients with stage 3 CKD (GFR 30-59 mL/min/1.73 m2) as defined internationally, diagnosed using Modification of Diet in Renal Disease/Chronic Kidney Disease Epidemiology Collaboration (MDRD/CKD EPI) eGFR (at least two consecutive test results in this range at least 90 days apart, with the most recent test in the last 12 months)
3. Written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 1320; UK Sample Size: 1320

Key exclusion criteria
1. History of untoward reactions to iodinated contrast media or allergy to topical iodine
2. Episode of acute kidney injury in previous 6 months (as defined by the Acute Kidney Injury Network criteria)
3. Amputation of whole or part limb
4. Pregnant or breastfeeding
5. Known alcohol or drug abuse
6. Any clinical condition with an expected survival of less than study duration
7. Inability to comply with study schedule and follow-up
8. Inability to provide informed consent e.g. due to cognitive impairment

Date of first enrolment
01/02/2014

Date of final enrolment
31/07/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Birmingham Clinical Trials Unit
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University of Birmingham
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Sponsor information

Organisation
University of Birmingham (UK)

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Sponsor type
University/education

Website
http://www.birmingham.ac.uk

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
NIHR Health Technology Assessment Programme - HTA (UK)

Results and Publications

Publication and dissemination plan
There will be three different sets of results:
1. A substudy (BVS – biological variability), which has been submitted for publication in 2019.
2. The first primary outcome, accuracy of eGFRs, will be submitted for publication in 2020.
3. The second primary outcome, comparison of eGFRs for monitoring disease progression (over the 3 years of study follow up) will be submitted for publication in 2021.

Intention to publish date
30/06/2021

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?
Protocol article		14/01/2014		Yes	No

Results article	01/08/2019	10/08/2020	Yes	No
HRA research summary		28/06/2023	No	No
Results article	01/07/2024	29/07/2024	Yes	No