

A cohort study of haemodialysis patients based on hepatic magnetic resonance imaging

Submission date 20/05/2011	Recruitment status Stopped	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 14/06/2011	Overall study status Stopped	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 13/09/2022	Condition category Urological and Genital Diseases	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

The aim of this study is to use a technique called quantitative magnetic resonance imaging (MRI) to measure the iron content of the liver, spleen, heart and pancreas and also liver fat fraction of patients who are undergoing hemodialysis or peritoneal dialysis, at the start of dialysis and thereafter when they are being treated with intravenous iron and erythropoiesis stimulating agents (ESA). The study will also find out about the risk factors of iron overload, and especially the role of iron therapy.

Who can participate?

Patients undergoing hemodialysis three times a week, home hemodialysis or peritoneal dialysis at the initiation of the technique and thereafter

What does the study involve?

MRI is used to determine the iron content of the participants' liver, spleen, heart, pancreas and also liver fat fraction. The participants' medical records and dialysis charts are reviewed by clinical research technicians. Blood samples are taken and the patients are tested for measurement of biochemical markers of iron metabolism and for a genetic defect of the HFE genes. A test is carried out to determine the participants' alcohol consumption and to detect alcohol addiction. Patients are followed up for analysis of relevant clinical events (illness and death).

What are the possible benefits and risks of participating?

Careful monitoring of iron therapy will allow the safe use of intravenous iron, avoiding iron overload. The risks of participating are anxiety related to MRI exams and genetic testing.

Where is the study run from?

Hôpital Privé Claude Galien (Quincy sous Sénart), Centre Hospitalier Marc Jacquet (Melun), Groupe Hospitalier Pitié Salpêtrière (Paris), Groupe Hospitalier Kremlin Bicêtre (Kremlin Bicêtre), Centre Nephrocare (Marne la Vallée), Polyclinique des Mousseaux (Evry), Clinique du Landy (St Ouen), Polyclinique les Fleurs (Ollioules), CHU Brabois (Nancy), Clinique Sainte Anne (Strasbourg), CH (Mulhouse), Hôpital Jean Mermoz (Lyon), Polyclinique du Plateau (Bezons)

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

January 2005 to January 2035

Who is funding the study?

The Physicians' Association of Claude Galien Hospital (Association Quincy Recherche Clinique et Thérapeutique) (France)

Who is the main contact?

Dr Guy Rostoker

rostotom@orange.fr

Contact information

Type(s)

Scientific

Contact name

Dr Guy Rostoker

ORCID ID

<http://orcid.org/0000-0002-4383-3825>

Contact details

Service de Néphrologie et de Dialyse

Hopital Privé Claude Galien

20 route de Boussy

Quincy Sous Senart

France

91480

-

rostotom@orange.fr

Type(s)

Scientific

Contact name

Ms Mireille Griuncelli

Contact details

Service de Néphrologie et de Dialyse

Hôpital Privé Claude Galien

20 route de Boussy

Quincy-sous-Sénart

France

91480

-

rostotom@orange.fr

Type(s)

Scientific

Contact name

Ms Christelle Loridon

Contact details

Service de Néphrologie et de Dialyse
Hôpital Privé Claude Galien
20 route de Boussy
Quincy-sous-Sénart
France
91480
-
rostotom@orange.fr

Additional identifiers**EudraCT/CTIS number**

Nil known

IRAS number**ClinicalTrials.gov number**

Nil known

Secondary identifying numbers

Nil known

Study information**Scientific Title**

Analysis of hepatic iron stores of haemodialysis patients by magnetic resonance imaging: a cross-sectional and longitudinal study

Study objectives

The aim of this study was to determine hepatic iron content, using magnetic resonance imaging (MRI) and the Rennes University algorithm, in a cohort of haemodialysis patients receiving both intravenous iron and erythropoiesis stimulating agents (ESA), in keeping with current guidelines.

Ethics approval required

Old ethics approval format

Ethics approval(s)

1. COMEDIMS (Drug, Devices and Clinical Trials Committee) CHP Claude Galien, 09/12/2004, ref: 2004-2
2. COMEDIMS (Drug, Devices and Clinical Trials Committee) CHP Claude Galien, 15/02/2013, ref 2013-2

Study design

Prospective cross-sectional longitudinal multicenter study

Primary study design

Observational

Secondary study design

Cross-sectional longitudinal study

Study setting(s)

Hospital

Study type(s)

Diagnostic

Participant information sheet

Not available in web format, please contact rostotom@orange.fr to request a patient information sheet

Health condition(s) or problem(s) studied

Chronic kidney disease

Interventions

Current interventions as of 08/09/2016:

1. Non-randomised measurement of hepatic iron content by means of T1 and T2 contrast magnetic resonance imaging (MRI) on a Sigma MRI unit (GE Medical Systems, Milwaukee, WI, USA) operating at a field strength of 1.5 Tesla
2. Five weighted gradient-recalled-echo sequences of the liver (GRE T1, DP, T2, T2+ and T2++) with a repetition time of 120 ms will be acquired
3. Measurements will be made in five regions of interest larger than 1 cm² (usually 3 on the right liver and 2 on paraspinal muscles on the same slice), and calculated the liver-to-muscle ratio
4. Areas of cyst-free liver will be examined in patients with renal and hepatic polycystosis
5. We will use the software algorithm provided by Rennes University (<http://www.radio.univ-rennes1.fr>) to determine hepatic iron content (expressed in micromol/g of dry liver)
6. Duration of MRI examination is about 20 minutes
7. Measurements of biochemical markers of iron metabolism:
 - 7.1. Serum ferritin
 - 7.2. Serum iron
 - 7.3. Transferrin
 - 7.4. Transferrin saturation (TSAT)
 - 7.5. Soluble transferrin receptors (sTfR)
 - 7.6. Serum hepcidin-25
 - 7.7. Screening for the C282Y HFE gene mutation
 - 7.8. Serum hepcidin-20, 22, and 24
 - 7.9. Serum erythroferrone
 - 7.10. Serum glycosylated ferritin
 - 7.11. Serum non bound transferrin iron (NBTI) and serum labile iron
 - 7.12. Plasma FGF23 C-terminal, plasma FGF23 Intact, soluble alpha Klotho, sclerostin
8. Use of The Alcohol Use Disorder Identification Test (AUDIT) to quantify alcohol consumption and to detect addiction
9. Measurement of iron content in spleen and heart will be performed simultaneously to determination of liver iron content by R2* relaxometry
10. Follow-up of patients for relevant clinical events (morbidity and mortality)

Added 23/10/2018: Measurement of liver fat fraction by R2* relaxometry with IDEAL IQ algorithm and Rennes University Gandon's algorithm and measurement of iron content in pancreas by R2* relaxometry

Previous interventions from 01/03/2013 to 08/09/2016:

1. Non-randomised measurement of hepatic iron content by means of T1 and T2 contrast magnetic resonance imaging (MRI) on a Sigma MRI unit (GE Medical Systems, Milwaukee, WI, USA) operating at a field strength of 1.5 Tesla
2. Five weighted gradient-recalled-echo sequences of the liver (GRE T1, DP, T2, T2+ and T2++) with a repetition time of 120 ms will be acquired
3. Measurements will be made in five regions of interest larger than 1 cm² (usually 3 on the right liver and 2 on paraspinal muscles on the same slice), and calculated the liver-to-muscle ratio
4. Areas of cyst-free liver will be examined in patients with renal and hepatic polycystosis
5. We will use the software algorithm provided by Rennes University (<http://www.radio.univ-rennes1.fr>) to determine hepatic iron content (expressed in micromol/g of dry liver)
6. Duration of MRI examination is about 20 minutes
7. Measurements of biochemical markers of iron metabolism:
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 - 7.4. Transferrin saturation (TSAT)
 - 7.5. Soluble transferrin receptors (sTfR)
 - 7.6. Serum hepcidin-25
 - 7.7. Screening for the C282Y HFE gene mutation
8. Use of The Alcohol Use Disorder Identification Test (AUDIT) to quantify alcohol consumption and to detect addiction
9. Measurement of iron content in spleen and heart will be performed simultaneously to determination of liver iron content by R2* relaxometry
10. Follow-up of patients for relevant clinical events (morbidity and mortality)

Previous interventions from 07/12/2012 to 01/03/2013:

1. Non-randomised measurement of hepatic iron content by means of T1 and T2 contrast magnetic resonance imaging (MRI) on a Sigma MRI unit (GE Medical Systems, Milwaukee, WI, USA) operating at a field strength of 1.5 Tesla
2. Five weighted gradient-recalled-echo sequences of the liver (GRE T1, DP, T2, T2+ and T2++) with a repetition time of 120 ms will be acquired
3. Measurements will be made in five regions of interest larger than 1 cm² (usually 3 on the right liver and 2 on paraspinal muscles on the same slice), and calculated the liver-to-muscle ratio
4. Areas of cyst-free liver will be examined in patients with renal and hepatic polycystosis
5. We will use the software algorithm provided by Rennes University (<http://www.radio.univ-rennes1.fr>) to determine hepatic iron content (expressed in micromol/g of dry liver)
6. Duration of MRI examination is about 20 minutes
7. Measurements of biochemical markers of iron metabolism:
 - 7.1. Serum ferritin
 - 7.2. Serum iron
 - 7.3. Transferrin
 - 7.4. Transferrin saturation (TSAT)
 - 7.5. Soluble transferrin receptors (sTfR)
 - 7.6. Serum hepcidin-25
 - 7.7. Screening for the C282Y HFE gene mutation
8. Use of The Alcohol Use Disorder Identification Test (AUDIT) to quantify alcohol consumption and to detect addiction

9. Measurement of iron content in spleen and heart will be performed simultaneously to determination of liver iron content by T2*/R2* sequences

Previous interventions until 07/12/2012:

1. Non-randomised measurement of hepatic iron content by means of T1 and T2 contrast magnetic resonance imaging (MRI) on a Sigma MRI unit (GE Medical Systems, Milwaukee, WI, USA) operating at a field strength of 1.5 Tesla
2. Five weighted gradient-recalled-echo sequences of the liver (GRE T1, DP, T2, T2+ and T2++) with a repetition time of 120 ms will be acquired
3. Measurements will be made in five regions of interest larger than 1 cm² (usually 3 on the right liver and 2 on paraspinal muscles on the same slice), and calculated the liver-to-muscle ratio
4. Areas of cyst-free liver will be examined in patients with renal and hepatic polycystosis
5. We will use the software algorithm provided by Rennes University (<http://www.radio.univ-rennes1.fr>) to determine hepatic iron content (expressed in micromol/g of dry liver)
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7. Measurements of biochemical markers of iron metabolism:
 - 7.1. Serum ferritin
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 - 7.3. Transferrin
 - 7.4. Transferrin saturation (TSAT)
 - 7.5. Soluble transferrin receptors (sTfR)
 - 7.6. Serum hepcidin-25
 - 7.7. Screening for the C282Y HFE gene mutation
8. Use of The Alcohol Use Disorder Identification Test (AUDIT) to quantify alcohol consumption and to detect addiction

Intervention Type

Other

Phase

Not Applicable

Primary outcome measure

1. Determination of iron content (micromol/g/dry weight)
2. Percentage of patients with abnormal iron liver content (mild, moderate and severe overload)
3. As hepatic MRI accurately detects liver iron overload exceeding 50 micromol/g, the upper limit of normal was set at 50 micromol/g for this study
4. Values between 51 and 100 micromol/g will be considered to represent mild iron overload, values between 101 and 200 micromol/g moderate iron overload; and values >201 micromol/g severe iron overload.
5. MRI for quantification of hepatic iron stores will be performed (as possible) at least seven days after iron infusion

Added 18/07/2013:

6. Spleen involvement
7. Heart (cardiac) involvement

Added 23/10/2018:

8. Liver fat fraction measured by R2* relaxometry with IDEAL IQ algorithm and Rennes University Gandon's algorithm, and iron content in pancreas measured by R2* relaxometry

Secondary outcome measures

1. Analysis of factors determining iron content:
 - 1.1. Demographic characteristics
 - 1.2. Clinical variables
 - 1.3. Dialysis vintage
 - 1.4. Erythropoiesis-stimulating agents (ESA) and iron therapies
 - 1.5. AUDIT score
 - 1.6. Mutation of HFE gene
2. Relationship between hepatic iron content and biochemical makers of iron status and hepcidine-25

Overall study start date

31/01/2005

Completion date

01/01/2035

Reason abandoned (if study stopped)

This study was stopped at the end of February 2020 due to the COVID-19 pandemic.

Eligibility

Key inclusion criteria

1. Patients of either sex
 2. Undergoing chronic intermittent bipuncture bicarbonate hemodialysis (with ultrapure dialysate single use biocompatible membranes) three times a week
- Added 18/07/2013: 3. or peritoneal dialysis
- Added 23/10/2018: 4. At initiation of dialysis and with longitudinal follow-up

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

600

Total final enrolment

411

Key exclusion criteria

1. Refusal to participate in the study
2. Poor compliance with the dialysis therapy schedule

3. Age < 18 years
4. Severe cognitive impairment
5. Claustrophobia
6. Hepatic cirrhosis
7. Overt inflammatory or infectious disease
8. Malnutrition
9. Recent major bleeding (< 3 months), major surgery (< 3 months), transfusion dependency, recent transfusion (< 3 months)
10. Intractable malignancy
11. Cardiac pacemakers and metallic cardiac valves

Date of first enrolment

01/03/2005

Date of final enrolment

31/01/2025

Locations

Countries of recruitment

France

Study participating centre

Hopital Privé Claude Galien

France

-

Study participating centre

Hôpital de Melun

France

-

Study participating centre

Groupe Hospitalier Pitié-Salpêtrière

France

-

Study participating centre

Groupe Hospitalier Kremlin Bicêtre

France

-

Study participating centre
Centre Nephrocare Marne la Vallée
France
-

Study participating centre
Polyclinique des Mousseaux
France
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Study participating centre
Clinique du Landy
France
-

Study participating centre
Polyclinique les Fleurs
France
-

Study participating centre
Hôpital de Mulhouse
France
-

Study participating centre
Polyclinique du Plateau, Bezons
France
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Study participating centre
Clinique Saint-Anne de Strasbourg
France
-

Study participating centre

CHU de Nancy

France

-

Study participating centre

Hôpital Privé Jean Mermoz

Lyon

France

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Sponsor information

Organisation

Quincy Association of Clinical Research and Therapeutics (non profit association, France)

Sponsor details

Association Quincy Recherche Clinique et Therapeutique (QRCT) (France)

4 Rue du Moulin de Jarcy

Quincy Sous Senart

France

91480

-

rostotom@orange.fr

Sponsor type

Research council

Funder(s)

Funder type

Hospital/treatment centre

Funder Name

Physicians Association of Claude Galien Hospital (Association Quincy Recherche Clinique et Thérapeutique - QRCT) (France)

Results and Publications

Publication and dissemination plan

The plan is to publish in 2016:

1. A study on iron stores in peritoneal dialysis patients (last patient included in December 2015)
2. A study on the relationship between liver iron concentration at MRI and HFE mutations C282Y, H63D and S65C

The plan is to publish in 2017 :

1. A replication multicentre study on iron overload in hemodialysis patients (replication of the original monocenter study published in the Am J Med in 2012)
2. A multicentre study for research of heart iron deposits in hemodialysis patients

Added 23/10/2018:

The plan is to publish in 2021:

1. A replication multicentre study on iron overload in hemodialysis patients (replication of the original monocenter study published in the Am J Med in 2012)
2. A monocenter study (Claude Galien, Quincy) for research of pancreatic iron deposits in dialysis patients
3. A multicentre study for research of heart iron deposits in hemodialysis patients

Intention to publish date

Individual participant data (IPD) sharing plan

Participant-level data are already available as a supplemental file of the following published article: <http://www.ncbi.nlm.nih.gov/pubmed/25506921>

These participant-level data are common with the other published article: <http://www.ncbi.nlm.nih.gov/pubmed/26182077>

The trialists also wish to make the participant-level data available for their next planned publications.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2012		Yes	No
Results article	results	15/12/2014		Yes	No
Results article	results	16/07/2015		Yes	No
Results article	results	05/01/2017		Yes	No
Results article	results	01/07/2017		Yes	No
Results article	results	23/07/2017		Yes	No
Results article	results	21/11/2017		Yes	No
Results article	results	01/01/2019		Yes	No
Results article	Calcific uremic arteriolopathy analysis in the total final 358 dialysis patients	23/01/2021	13/09/2022	Yes	No

[Results
article](#)

Results

05/07
/2022

13/09
/2022

Yes

No