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

Submission date	Recruitment status	[_] Prospectively registered
20/05/2011	Stopped	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
14/06/2011	Stopped	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
13/09/2022	Urological and Genital Diseases	[_] 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?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
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

Study type(s)
Diagnostic

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 used 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, sclerotin
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 used the software algorithm provided by Rennes University (http://www.radio.univ-

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7.1. Serum ferritin
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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 used 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 used 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

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
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

Key secondary outcome(s))
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

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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-Salpétrière
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
-

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
-

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
-

Sponsor information

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

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

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
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes