

Title:	Assessment of liver iron by R2 – MRI data analysis	
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Aim

To assess the safety, effectiveness and cost-effectiveness of the monitoring and quantification of iron levels in the liver by R2-MRI data analysis in patients with, or suspected of, systemic iron overload due either to hereditary (primary) haemochromatosis; or secondary iron overload (commonly a consequence of repeated blood transfusions).

The pattern of distribution of iron varies between patients with iron overload due to primary haemochromatosis (increased iron from the gastrointestinal tract) or transfusional iron overload. For this reason these populations were treated separately in the assessment report. The current direct method to assess the extent of iron overload in the liver is by liver biopsy. Patients with primary haemochromatosis who have iron overload in the liver are at high risk of liver disease (e.g., cirrhosis) an important prognostic implication for risk of hepatocellular carcinoma and survival. Patients who require routine monitoring of liver iron levels due to repeated transfusions are, because of the pain and side effects associated with liver biopsy, usually monitored by indirect methods, such as serum ferritin levels. R2-MRI data analysis is unlikely to have an impact on the utilisation of indirect methods.

Results and Conclusions

Safety

R2-MRI data analysis is a software application that interprets data captured by MRI and has no direct interaction with the MRI scanner, patient or environment. There were no reports located that specifically investigated the safety of R2-MRI analysis but it would be reasonable to assume that there is no adverse events associated with the use of the software. There may be safety concerns with the use of the MRI scan itself — particularly, regular repeated MRI scans but it has been generally accepted as a 'safe' imaging modality as MRI does not involve ionising radiation, as long as proper precautions are taken. By comparison, liver biopsy is an invasive and painful procedure, and carries the risk of bleeding and infection, and damage to the liver or surrounding organs. The safety of liver biopsy is enhanced by ultrasound guidance. Assessment of hepatic iron concentrations (HIC) by R2-MRI data analysis is likely to be associated with safety advantages when compared with assessment of HIC by liver biopsy.

Effectiveness

Only one study was identified, a diagnostic case control study (level III-2). This study had two purposes: it derived a calibration curve to determine HIC from an average liver R2 value; and it compared HIC as estimated by R2-MRI data analysis with HIC as estimated by chemical assay of liver specimen obtained by needle biopsy. Key uncertainties were noted with respect to the evidence. Firstly, in the identified study, the same set of data is used to derive the calibration curve to convert average liver R2 measurements to an HIC and to compare the HIC values estimated using R2-MRI data analysis with the HIC values estimated by chemical assay of a liver sample collected by needle biopsy. Although the derived calibration curve could form the basis for a hypothesis of the relationship between HIC and R2 values, for the validity of the relationship to be accepted, assessments of HIC by liver biopsy and by liver R2 values should be conducted in a separate group of patients and the same relationship found to apply. Secondly, the study found that because the mean relative difference between HIC estimated by R2-MRI data analysis and HIC estimated by the liver biopsy is not significantly different from zero, the single derived calibration curve will be sufficient to model the relationship between liver R2 and HIC for all subject groups. However, the finding that the mean relative difference is not significantly different from zero is not surprising because the same data are used to generate the calibration curve as to assess the relative difference between R2-MRI HIC and liver biopsy HIC.

There is substantial uncertainty around the validity of the specific mathematical relationship assumed to exist. The benefit to clinicians of converting R2 values to HIC has to be weighed against the potential for false confidence in the accuracy of the HIC value generated. It was proposed that specification of reference ranges for R2 would be more helpful than conversion of R2 values to HIC.

Economic evaluation

As assessment of HIC by R2-MRI data analysis will generally substitute for assessment of HIC by chemical assay of a liver biopsy sample a comparative costs analysis of the two procedures was done. With FerriScan®, a telemedicine model is adopted, whereby data are transmitted to a central data analysis facility as a digital specimen to be analysed. Following analysis at the central facility, a report detailing results is returned to the radiologist at the centre where the MRI was conducted. The cost per assessment assumed a cost for the MRI component of the intervention as well as a fee for the computerised quantitative analysis of data collected by MRI. In estimating the MBS items likely to be associated with assessment of HIC by liver biopsy, it was noted that although the safety of liver biopsy is enhanced by ultrasound guidance and that in practice it is likely that this procedure would be done under ultrasound guidance, no specific MBS item for ultrasound guided liver biopsy is included. Liver biopsy is generally performed under sedation in a hospital; therefore costs associated with hospitalisation also need to be taken into account when taking a health care system perspective. The assessment of HIC by R2-MRI data analysis is likely to be cost-saving from a health care perspective compared with assessment of HIC by liver biopsy. However, since costs of hospitalisation are not borne by the MBS, the assessment of HIC by R2-MRI data analysis is likely to be more costly to the MBS than liver biopsy.

Methods

The evidence regarding the use of R2-MRI data analysis to monitor and quantify levels of iron in the liver was systematically assessed. PubMed was searched from 1950-June 2009. EMBASE, Cochrane DSR, ACP Journal Club, CCTR, HTA and NHSEED were searched for relevant literature from inception of the databases to July 2009. Studies were included in the review on the basis of pre-determined PICO selection criteria and reasons for exclusion were documented. Study quality was appraised, using appropriate checklists, data were extracted in a standardised manner, and results were reported in a structured narrative.