All corrections made in the text itself appear in blue as well as responses to reviewers.

Reviewer #1:

Specific Comments to Authors: In this work, the authors described the plasma and urinary concentrations of iohexol systematically using rich kinetics of samples collected over 24 hours in cirrhotic patients with 3 different grades of ascites, then try to build a Bayesian estimator to simplify the estimation of mGFR. However, there are major specific points in this manuscript as shown in following comments: 1. Iohexol could damage renal tubulointerstitium and affect renal function, is it scientific and reasonable to use iohexol for research in this pilot study? Please explain it. 2. It is recommended that the research cases should be added for the study. 3. It is recommended that adding experiments of endogenous creatinine clearance rate for comparative study in this work.

1) Iohexol could damage renal tubulointerstitium and affect renal function, is it scientific and reasonable to use iohexol for research in this pilot study?

Apart from effects of an immuno-allergic nature or reaction at the puncture site, the very low doses used for pharmacokinetics make the other side effects described during the use of iohexol as an iodinated contrast product very unlikely ((10) Delanaye, PMID: **27679715)**. Please see this reference review of publications on the subject.
Iohexol, a non-ionic contrast agent, is most suited to replace inulin as the marker of choice for GFR determination. Iohexol comes very close to fulfilling all requirements for an ideal GFR marker in terms of low extra-renal excretion, low protein binding and in being neither secreted nor reabsorbed by the kidney. In addition, iohexol is virtually non-toxic and carries a low cost. Moreover, iohexol is stable in plasma. The safety of iohexol has been extensively studied and is confirmed by the large number of iohexol measurements performed in different countries. No severe adverse event, and particularly no anaphylactic reaction, occurred. This safety profile is, at least in part, explained by the current low dose of iohexol injected (5 or 10 mL versus 80–180 mL for CT scan and 130–300 mL for coronary interventions) and by the exclusion of patients with known contrast medium reactions. Even in patients with minimal renal function, iohexol doses of 10 mL (300 mg I/mL) have not been shown to be nephrotoxic. Many publications are available on the subject.
Finally, the performance of iohexol clearance has been approved by our ethics committee for this protocol.
Please, see explanations in the discussion page 11.

2) It is recommended that the research cases should be added for the study.

The Patient's main characteristics are described in table 1 and for each patient studied, the proportion of the iohexol administered dose detectable as a function of time in plasma and urine is given in figure 1.

3) It is recommended that adding experiments of endogenous creatinine clearance rate for comparative study in this work

Creatinine being produced from creatine by hepatic metabolism, an hepatic dysfunction would so result in a dysfunction in creatinine production leading to a great difficulty to differentiate renal and liver dysfunction part.Moreover, creatinine is secreted in small quantities by the target tubules, which therefore implies a slight increase in the glomerular filtration rate during the measurements. Therefore, we preferred to measure the GFR with exogenic substances which are considered as the reference such as inulin and now iohexol or Cr-EDTA.

Finally, the Brochner Mortensen formula has been described as a very accurate marker of creatinine clearance in other populations and has been calculated in the present study allowing a comparison to the true theoretical endogeneous creatinine clearance rate.

Reviewer #2: This was a pilot study, which investigated the role of iohexol as a marker of renal function in a small group of patients with cirrhosis. The topic is of interest because, as the Authors stated in the Introduction section, serum creatinine may not adequately reflect the true renal function in patients with cirrhosis. Moreover, creatinine has been used in several fields in cirrhosis, for instance into the MELD score (or MELD NA score) which is widely used to grant prioritization to liver transplantation. The main finding of this study was that iohexol concentrated in the urines with an inverse behavior of the plasma curves, confirming the fact that this molecule is filtered by the glomerulus, and not reabsorbed or secreted by the tubule. However, the whole dose of infused iohexol was not found in urines in 100% patients. Therefore, the study did not fully elucidate if iohexol may be a good marker of renal function in cirrhosis. - I suggest to add a control group made of patients without cirrhosis - The hypothesis of iohexol concentration in ascites should be confirmed by including a large number of patients with ascites undergoing paracentesis - The Authors said that urine collection was quite difficult for some patients, and could be difficult in clinical practice. I think that this could be a minor issue, for instance using an urometer in hospitalized patients. - Did the patients withdraw diuretics during measurements? - I appreciate the section where the Authors clearly described pitfalls of this study, which is a pilot experience needing further investigations. - Statistical analysis is good as well as tables and figures

1) I suggest to add a control group made of patients without cirrhosis

   We thank the reviewer for this very judicious remark. Unfortunately, for reasons of logistical and budgetary constraints concerning healthy patients, it was difficult for us to propose this control population. However, we can add in the discussion () the data of the existing literature on iohexol.
   Five studies were interested in the measurement of the clearance of iohexol in healthy population, 5 in the plasma and 2 in the urine and this, in comparison with the reference methods.
   The first by Sterner et al. ((20), PMID: **17943640**) compared the performance of plasma and renal clearance estimated by iohexol vs inulin in 20 healthy patients. They took 2 urine samples (5-6h and 6-7h) and obtained results comparable to inulin. The second, Brown and O'Reilly ((21), PMID: **1875470**) performed roughly the same study and obtained comparable results.
   If we consider that we recover 100% of inulin in a healthy patient and that we obtain the same renal clearance with iohexol we can assume that we recover 100% of iohexol in a healthy population even if in none of these 2 studies, the authors present the results of the dose collected in the urine. Please, see comments in the discussion page 15.

2) The hypothesis of iohexol concentration in ascites should be confirmed by including a large number of patients with ascites undergoing paracentesis
   We completely agree and intend to perform this in the future study aiming to build a Bayesian estimator.

3) Urine collection was quite difficult for some patients. I think that this could be a minor issue, for instance using an urometer in hospitalized patients.
   We agree with this proposal and add it for the study aiming to build a Bayesian estimator. Please see page 11.

4) Did the patients withdraw diuretics during measurements?

Yes this precaution was systematic taken for the study we add it in the method. Please see page 7.

(1) Science editor:

Authors showed the result of pilot prospective study of iohexol use to estimate renal function for cirrhotic patients. This study suggested that iohexol might be a useful marker. It is an interesting study, but several issues remains to be addressed. Revise according to reviewers7 comments is required. Authors should assess the safety profile carefully. Data about detail renal function after iohexol administration should be shown and be discussed.

Authors should assess the safety profile carefully. Data about detail renal function after iohexol administration should be shown and be discussed.

Please see comment to reviewer 1

Apart from effects of an immuno-allergic nature or reaction at the puncture site, the very low doses used for pharmacokinetics make the other side effects described during the use of iohexol as an iodinated contrast product very unlikely ((10) Delanaye, PMID: **27679715)**. Please see this reference review of publications on the subject.
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Finally, the performance of iohexol clearance has been approved by our ethics committee for this protocol.
Please, see explanations in the discussion page 11.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Hepatology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the

author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content. Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

We have corrected all form issues as requested.