Author's response to reviews

Title: The accuracy of the report of hepatic steatosis on ultrasonography in a clinical setting: A retrospective observational study

Authors:

Matthew J Hepburn (matthew.hepburn@us.army.mil)
Jeffrey A Vos (jeffrey.vos@amedd.army.mil)
Eric P Fillman (eric.fillman@amedd.army.mil)
Eric J Lawitz (lawitz@alamomedicalresaearch.com)

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Author's response to reviews: see over
Dear Editors,

We appreciate the insightful review of our manuscript. We have carefully considered the comments of the reviewer, and modified the manuscript based on these suggestions. Our specific responses to the reviewer’s comments are below:

1. **Hepatitis C should be included in the title.** We agree with the reviewer’s comment, and have changed the title. The revised title is ‘The accuracy of the report of hepatic steatosis on ultrasonography in patients infected with hepatitis C in a clinical setting: A retrospective observational study.’

2. **It would make the most sense to include only patients with ultrasound and biopsy. Why include those who had no biopsy?**

   Our study had two purposes: to describe the type of patient that is more likely to have steatosis described on ultrasound, and then to compare steatosis on ultrasound vs. steatosis on biopsy. For the first purpose, we include all patients with hepatitis C who had ultrasounds performed. Some of these patients did not have biopsies. We discovered some interesting associations, such as the correlation between steatosis on ultrasound and ALT. We are not sure if there is a compelling reason to exclude patients without a biopsy from this analysis. Including these patients allowed for the maximum number of available patients to be analyzed (169 subjects instead of 122 subjects). It also decreased selection bias, as patients who both accepted and declined biopsy were incorporated into the initial analysis.

   We would prefer not to re-analyze the data with a lower sample size, without a convincing reason to exclude them. We will re-analyze if the Editors request it.

   We have modified the manuscript to clarify the difference between analyzing all subjects with ultrasound results and analyzing ultrasound vs. biopsy results. Hopefully, these changes will clarify why all patients should be included in the analysis of clinical/laboratory factors associated with steatosis on ultrasound.

   In the introduction, fifth paragraph, the following sentences were added:

   The first part of our analysis was to examine all patients who had hepatic ultrasonography performed, including patients who did not have a liver biopsy. The second part of our analysis (comparing steatosis on ultrasound report to steatosis on biopsy) included only patients who had hepatic ultrasonography and liver biopsy.

   The following sentence was also added to the conclusion:
Even patients who did not have a liver biopsy were included in the analysis of associations with steatosis, and the description of steatosis on ultrasound was associated with factors reflective of hepatic inflammation (such as ALT).

3. The ultrasound equipment used should be stated. Some equipment may be preferable to others for this purpose. We have clarified the type of ultrasonography equipment in the Methods section, under Ultrasonography:

The machines utilized in the Radiology Department were the ATL Ultramark HDI 3000® Ultrasound System and the ATL Ultramark HDI 5000® Ultrasound System.

4. Were there patients with focal fatty liver or focal fatty liver sparing? If so, was the biopsy directed?
The ultrasound reports did not specifically describe if the fatty liver was focal or diffuse, but rather only stated on the presence or absence of steatosis. Therefore, none of the biopsies were directed at steatotic portions of the liver. The following sentence was added to the Methods section, under Ultrasonography, to clarify this point:

Reports did not distinguish between diffuse or focal fatty liver.

5. What was the interval from ultrasound to biopsy? If it was long, weight change during that interval would be relevant. The exact interval between ultrasound and biopsy was not calculated in this study. Generally, ultrasonography and biopsy were within 1-2 months of each other, and no biopsy occurred more than six months after ultrasonography. The following sentences were added to the Methods section, in the Histologic Examination section:

Liver biopsies were generally performed within 1-2 months of hepatic ultrasound. There were no liver biopsies in this study utilized that were > 6 months after ultrasonography.

We acknowledge that it is possible that small changes in histology could have occurred in the time between ultrasound and biopsy. We have mentioned this issue in the limitations paragraph in the Discussion section with the following sentences:

Also, for some patients, there was time between the dates in which the ultrasound and biopsy were performed. It is possible that small changes in liver histology could have occurred, if the patient had significant weight gain or loss, for example.

Discretionary revisions:
1. **The authors may want to mention other imaging modalities that are better than ultrasound in detecting fat.** We have decided to mention these modalities in the Discussion section, with the following sentences:

Practitioners should rely on other diagnostic modalities to assess the liver for steatosis, including biopsy or other radiologic technologies. Magnetic resonance imaging or computerized tomography are two potential techniques that may be clinically useful in the diagnosis of hepatic steatosis pending further study.

**AND**

Until a superior non-invasive modality is proven to be superior in a clinical setting, liver biopsy remains the optimal diagnostic procedure for the determination of steatosis in patients infected with hepatitis C.

We are very willing to make any additional changes recommended by the reviewer or by the Editors.

Sincerely,

Matthew J. Hepburn, Major, Medical Corps, US Army  
PSC 821, Box 84  
FPO, AE 09421  
Office phone: 44 01980 613 929  
e-mail: matthew.hepburn@amedd.army.mil