Reviewer’s report

Title: Is hepatotropic contrast enhanced MR a more effective method in differential diagnosis of hemangioma than multi-phase CT and unenhanced MR?

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Reviewer: Takamichi Murakami

Reviewer’s report:

In this article, the authors tried to find the most effective diagnostic radiological features enabling the diagnosis of hemangiomas with atypical appearance in ultrasound (US) on the basis of multi-phase CT, unenhanced-MR and liver-specific contrast-enhanced MR.

Major Strengths

1. The authors compared BOPTA-MRI with dynamic CT and unenhanced MRI.

Major weakness

2. There were no quantitative analysis nor statistical analysis.

3. This study design was not appropriate. Usefulness of T2-weighted images for diagnosis of hemangioma is already well known. If the authors would like to evaluate usefulness of BOPTA-MRI, they should evaluate unenhanced MRI and BOPTA-MRI (unenhanced MRI plus BOPTA enhanced MRI). By this study design, they can show whether BOPTA can improve diagnosis of hemangioma or not.

Major Compulsory Revisions

Abstract

3. Background

“hemangiomas with atypical appearance in ultrasound (US)”. The authors should clarify what is “atypical appearance”.


“Radiological features of lesions were evaluated by three independent observers.”

Though three independent observers evaluated, why did the authors show only consensus data in the text?

Introduction

5. The first paragraph. “However, high percentage of hemangiomas are nonspecific in US [3,4] and therefore it is necessary to introduce diagnostic procedures based on the use of new organ-specific contrast agents into the diagnostic algorithm.”
I can’t agree with this. Now, unenhanced and enhanced MRI with Gd-DTPA are widely used and useful.

6, The second paragraph. “... but reports on radiographic characteristics of hepatic lesions in MR imaging without and after liver-specific contrast administration are rarely encountered [5,6].” There are many papers about radiographic characteristics of hepatic lesions in MR imaging without.

Materials and Methods

7, The first to third paragraphs. “161 consecutive patients with non-specific hepatic masses observed in US were included in this prospective study…….398 focal liver lesions were evaluated. All lesions were divided into two groups. The first group (HH group) consisted of 99 hepatic hemangiomas, recognized in 34 patients. 21 patients with HH had isolated ….were recognized in 13 people. The second group (nonHH group) included 299 focal liver lesions other than hemangioma: …”

The authors stated that they evaluate 161 consecutive patients with non-specific hepatic masses. Did all the 99 hepatic lesions in the 161 consecutive patients population show “hepatic hemangiomas with atypical findings”? Was there no hemangioma with typical finding?

8, The fourth paragraph. “final diagnosis was based upon the histopathological examination”. How to get histological materials. Biopsy? Surgical?

9, The fifth paragraph. “In the remaining 61 patients, the final diagnosis was based upon the clinical and diagnostic imaging follow-up.” What kind of imaging modalities were employed for the follow up study? When the follow up examinations were performed? What kind of imaging findings on each modality were employed for final diagnosis of FNH, hemangioma, and metastases.

10, The sixth to seventh paragraphs. HAP, PVP, EP and DP should be spelled out because they appear initially. The scan timing of PVP and EP after an injection of contrast medium should be stated.

11, The eighth paragraph. “Spiral CT and MR images were then interpreted by three experienced investigators (ES,AS,MS).” The authors didn’t show data of each observers. Was this a consensus reading? When did they interpret each imaging modalities? At the time of blind reading, the observers should interpret each imaging modalities at least two week intervals to decrease memory bias.

12, The third paragraph from the end of Materials and Methods.

“Statistical analysis concerning characterization of hemangiomas …. has been performed with Statistica 8 (StatSoft Inc., Tulsa, OK, USA) and #2 test.Stastical analysis.” As this study compared each imaging modality in the same population, the authors should employed McNemar test, but not #2 test. Bonferroni compensation should also be performed because this is multiple comparison study.

There were no data of p value in the text. Did the authors perform statistical analysis?
Results
13, The first to the second paragraphs.

“Patient group consisted of 95 women and 66 men in the age of 18-79 years. The diameter of foci ranged from 6 mm to 125 mm (median 21 mm). According to the mean foci diameter, all lesions were divided into two groups: small lesions (<2cm) - 199 foci and large lesions (#2cm) - 199 foci. In the HH-group, 40 foci of cavernous hemagioma were large lesions and the rest of 59 tumors were small lesions.”

Who made this standard reference? Study coordinator? Who was Study coordinator?

The explanation how to made the standard reference should be stated in The Materials and Methods.

14, The fourth paragraph. “The type of enhancement in consecutive phases was similar in both CT and MR studies.” Was it similar or completely same?

Discussion
15, The first and second paragraph “Liver hemangioma ....(fig.10).” should be deleted because they were already reported in the previous papers. Figs. 8-10 should also be deleted.

16, The Discussion is too long and tediously. The authors just introduced previous papers’ data. Usefulness of T2-weighted images for diagnosis of hemangioma is already well known.

17, The fourth paragraph from the end of Discussion.

“Main restrictions of this study are lack of quantitative analysis of focal liver lesions signal intensity as described by other authors [37] due to a high occurrence of small foci and no incidence of giant hemangiomas (> 8cm) in which secondary changes like hemorrhage or hyalinization are more frequent [38].”

This can’t be a reason to justify lack of quantitative analysis. ROI can be placed on small lesion by magnifying images.

18, The third to the first paragraphs from the end of Discussion.

In BOPTA-MRI, we usually obtain both unenhanced images and enhanced images.

Even though T2-weighted imaging is usually useful for diagnosis of hemangioma, there are same lesions those are hard to diagnose. In such cases, whether an addition of BOPTA enhanced images to unenhanced images can improve diagnostic accuracy of hemangioma or not is important.

Tables
19, The authors should make an effort to reduce the number of Tables. 10 Tables are too much.

Figures
20, Figs. 1,2,3,8,9, and 10 should be deleted. The authors should show hemangioma with atypical signal intensity or enhancement pattern.

**Level of interest:** An article of insufficient interest to warrant publication in a scientific/medical journal

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.