

Reviewer #1

Overall, the article is informative and well written, and easy to understand. This is a new and very informative study for me. There are some minor mistakes that required to be removed to make it more comprehensive.

Response

We thank the reviewer for the comment. As suggested by other reviewers, we revised this manuscript carefully.

Reviewer #2

1, INTRODUCTION section: Reported carcinogenic risk factors after SVR are high aminotransferase (ALT) and α -fetoprotein (AFP) levels and low platelet levels [9]. The authors have reported that the velocity of shear waves (Vs) measured by shear wave elastography (SWE) is useful for diagnosing the level of fibrotic progression in hepatitis C and predicting carcinogenic risk [10, 11]. SWE is a new technology that measures liver stiffness by measuring the propagation velocity of shear waves generated in hepatic tissue [12]. The author should briefly describe the correlation between SWE and HCC here (predicting carcinogenic risk).

Response

We thank the reviewer for the insightful comments here and below. As suggested by the reviewer, we added the following sentences in INTRODUCTION section (page6, line14-18).

As for the carcinogenic patients, the liver stiffness measured by SWE at the beginning of DAAs treatment are high as compared with the non-carcinogenic patients. In addition, the liver stiffness is useful for the carcinogenic prediction than other parameters (AFP, Fib-4 index, ALT and platelet) at six months after the treatment.

2, MATERIALS AND METHODS/Patients section: Patients were treated with DAAs, and shear wave propagation velocity (Vs) was measured before treatment (baseline), at the end of treatment (EOT), and 12 weeks (follow-up 12) and 24 weeks..... The dose of DAAs should be described.

Response

We thank the reviewer for the comment. As suggested by the reviewer, we added the following sentences in MATERIALS AND METHODS/Patients section (page8, line2-8).

The treatment was provided according to guidelines on Japanese Society of Hepatology. Each duration of treatment was 8-12 weeks and the DAAs doses obeyed the package insert.

3, Did the HCCs confirmed by pathological examination?

Response

We thank the reviewer for the comment.

The HCC patients who had a diagnosis by a surgery specimen pathologically were 8/12 patients. Other 4 patients had a diagnosis of HCC by an imaging.

4, MATERIALS AND METHODS section: Identification of contributing factors for carcinogenesis in the medium-risk and high-risk groups. Parameters in which significant differences were seen were taken as explanatory variables..... What statistical method was used to analyze these parameters, Univariate analyses?

Response

We thank the reviewer for the comment. As suggested by the reviewer, we added the following sentences in MATERIALS AND METHODS/ Statistical analysis section (page10, line8-10).

A non-paired Wilcoxon test was used in comparisons of each parameter between the non-carcinogenic group and carcinogenic group.

5, The diagnostic performances of clinical parameters for predicting the presence of HCC were evaluated using receiver-operating characteristic (ROC) curve analyses. The statistical software "StatFlex version 7" was used in this study. Did the author want to establish a predictive model for predicting the occurrence of HCC based aMAP score and SWE? but after multiple regression analysis, a significant difference was seen only in Vs (P = 0.0296).

Response

We thank the reviewer for the comment. As suggested by the reviewer, the number of cases was not enough in this study, so we were not able to establish a predictive model for predicting the occurrence of HCC based aMAP score and SWE. Therefore, we focused on the stratification of the carcinogenic risk using aMAP score and Vs.

Reviewer #3

1. This is a single-center study with limited sample size included in the study and too few carcinogenic events, so statistical analysis may be biased, and the difference between the results is not significant, which needs to be further confirmed by increasing the sample size and extending the study time.

2. Due to the small number of carcinogenic events, the Cox proportional risk model was not adopted in this study, but multiple regression analysis was adopted, which was insufficient in the establishment and evaluation of risk model. It is suggested to enlarge the sample size and increase the follow-up time, and use cox analysis to further illustrate the demonstration.

Response

As suggested by the reviewer, this is a single-center study with limited sample size included in the study and too few carcinogenic events, so statistical analysis may be biased, and the difference between the results is not significant.

We understand that this study need to enlarge the sample size and increase the follow-up time, and use cox analysis to further illustrate the demonstration. However, patients with hepatitis C and the patients with hepatocellular carcinoma are in a tendency to decrease by the spread of DAAs therapy. Very long time is necessary for the expansion of enough sample sizes.

As suggested by the reviewer, it is innovative to annex aMAP score and Vs to evaluate a carcinogenic risk in hepatitis C patients. The authors strongly wish we report this viewpoint first in the world. Therefore we daringly submitted this manuscript with small number of cases.