Author’s response to reviews

Title: Long-term outcomes and risk factors of thyroid dysfunction during pegylated interferon and ribavirin treatment in patients with chronic hepatitis C infection in Taiwan

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Response to Editor Comments:

1) As you are using the National Health Insurance Research Database, please state in the Methods and Declarations (“Ethics approval and consent to participate”) whether the database is publicly available or not. If it is not, please include a statement that all necessary permissions were obtained to access and use the data and who gave this permission.

Answer: Thanks. We had added the sentence “We used the National Health Insurance Research Database in this study. According to the regulation of Ministry of Health and Welfare, Taiwan, all of the datasets are only available from the information Center, Ministry of Health and Welfare, Taiwan. The dataset was evaluated in the office of the Information Center and we handed out the results that we obtained. The datasets cannot be distributed by Information Center.” in Methods and declaration. (page 10, para 3, line 2; and page 20, para 2, line 2)

Response to Reviewer:
1. Authors should emphasize what is new in the present study more clearly.

Answer: We added the following description in discussion: “As our knowledge, this is the first study using National Health Insurance database to assess the relationship between thyroid dysfunction and pegylated interferon/ribavirin treatment in patients with chronic hepatitis C infection in Taiwan”. (page 14, para 2, line 1)

2. Text page 12, line 5: What was liver disease? All patients had chronic HCV infection.
Answer: The words “liver disease” should be “liver cirrhosis”. It had been corrected. (page 12, para 1, line 6 and table 1).

3. Text page 12, last line: "In the patients with TD, 173 (41.5%) had received antiviral drugs or interferon treatment…"; What were "antiviral drugs"? This term means that "antiviral drugs" were not IFN-based treatment. Furthermore, in next page 13 (line 3-4), "173 (4.5%) CHC patients who had been treated with PEG-IFN/RBV were diagnosed with TD…"; These descriptions were inconsistent.

Answer: Thank you for your comment. The words” antiviral drugs” were removed. The sentence was changed as: “173 (41.5%) had received PEG-IFN/RBV treatment, while 244 (58.5%) patients had not.” (page 12, para 3, line 4)

4. Sex was a significant factor in Table 3. However, in page 12 (line 16), sex was not associated with TD.

Answer: For making the statement clear, we added “Table 1” before the sentence and corrected as:” (Table 1) Compared to the nontreated group, the treated group had a higher rate of TD and lower rates of hypertension, diabetes, liver cirrhosis, and CKD.” (page 11, para 1, line 1)

5. Table 3, "Multivariate analysis" columns: Only the final step results should be denoted, and non-significant results should be deleted from the table. The definition of categorical data is obscure: for instance, "Hyperlipidemia (yes/no)" indicates that "no" has any fold hazard ratio against "yes". Which is "1 (standard)", "yes" or "no"?

Answer: Non-significant results were removed from table 3. We agree your opinion. The categorical data is obscure. We deleted the definition of hypolipidemia. Only definition of hyperlipidemia was remained in text. (Table 3; and page 10, para 2, line 5).

Response to Editor Comments:

1. Please state clearly the role the funder(s) had in your study in the "funding" section of the declarations.

   Answer: We added the following statement in the funding as: The funder had no role on the study design, data analysis, interpretation and writing the manuscript in this study. (page 21, para 3, line 2)

2. Figures should be attached to the manuscript as separate files, and each figure of a manuscript should be submitted as a single file.

   All figure titles/legends should be listed and placed at the end of the main manuscript, after the References, and not within any of the figure files.

   Answer: The figure had been put in separate file and legend was listed at the end of main manuscript.