

INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Concurrent hepatic steatosis increases the risk of hepatocellular carcinoma in patients with chronic hepatitis B or C virus infection: a systematic review and meta-analysis

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Review question / Objective: This review is designed to investigate the association between concurrent hepatic steatosis and the risk of HCC among patients with chronic hepatitis B or C virus infection.

Condition being studied: Nonalcoholic liver disease (NAFLD) is another important cause of chronic liver disease, with an estimated prevalence ranging from 17% to 33% in the general population. NAFLD comprises a wide disease spectrum ranging from simple steatosis to non-alcoholic steatohepatitis with or without fibrosis, which is associated with a high risk of progressing to cirrhosis and HCC. Moreover, HCV or HBV infection and hepatic steatosis are increasingly observed together due to the growing epidemic of obesity and type 2 diabetes. Several case-control and retrospective cohort studies have investigated the influence of concurrent hepatic steatosis on the risk of HCC among HCV or HBV-infected patients. However, the findings from such studies remain inconclusive. Such conflicting findings have raised concern as to whether hepatic steatosis is an independent risk factor of developing HCC among patients with HCV or HBV infection. This study is designed to investigate the association between concurrent hepatic steatosis and the risk of HCC among HCV-infected patients.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 July 2020 and was last updated on 21 July 2020 (registration number INPLASY202070099).

INTRODUCTION

Review question / Objective: This review is designed to investigate the association between concurrent hepatic steatosis and

the risk of HCC among patients with chronic hepatitis B or C virus infection.

Rationale: Chronic hepatitis C or B virus infection is a risk factor for hepatocellular

carcinoma (HCC). Hepatic steatosis is increasingly observed with chronic HCV or HBV infection. However, the impact of concurrent hepatic steatosis on the risk of HCC among HCV or HBV-infected patients remains inconclusive.

Condition being studied: Nonalcoholic liver disease (NAFLD) is another important cause of chronic liver disease, with an estimated prevalence ranging from 17% to 33% in the general population. NAFLD comprises a wide disease spectrum ranging from simple steatosis to non-alcoholic steatohepatitis with or without fibrosis, which is associated with a high risk of progressing to cirrhosis and HCC. Moreover, HCV or HBV infection and hepatic steatosis are increasingly observed together due to the growing epidemic of obesity and type 2 diabetes. Several case-control and retrospective cohort studies have investigated the influence of concurrent hepatic steatosis on the risk of HCC among HCV or HBV-infected patients. However, the findings from such studies remain inconclusive. Such conflicting findings have raised concern as to whether hepatic steatosis is an independent risk factor of developing HCC among patients with HCV or HBV infection. This study is designed to investigate the association between concurrent hepatic steatosis and the risk of HCC among HCV-infected patients.

METHODS

Search strategy: Search terms were ("fatty liver" OR "steatosis" OR "steatohepatitis") AND ("hepatitis C" OR "HCV") AND ("hepatocellular carcinoma" OR "HCC" OR "liver cancer" OR "Liver Neoplasm"). Databases included PubMed, Scopus, and Web of Science.

Participant or population: Patients with HCV or HBV infection.

Intervention: There is no intervention in this study because this meta-analysis is based on observational studies rather than randomised controlled studies. Basically, "HCV or HBV-infected patients with

concurrent hepatic steatosis" is corresponding to an "Intervention group".

Comparator: "HCV or HBV-infected patients without concurrent hepatic steatosis".

Study designs to be included: Case-control or cohort studies examining the association of hepatic steatosis with the risk of HCC among patients with HCV or HBV infection.

Eligibility criteria: (a) case-control or cohort studies examining the association of the presence of hepatic steatosis with the risk of HCC among patients with HCV infection; (b) all included studies should use odds ratios (ORs), risk ratios (RRs) or hazard ratios (HRs) with 95% confidence intervals (95% CIs) as the measure of effect size; (c) the diagnosis of hepatic steatosis was either based on histology or imaging.

Information sources: Electronic databases.

Main outcome(s): The outcome measure was the presence (or the occurrence during the follow up for cohort studies) of HCC among HCV-infected patients. The ORs, RRs, or HRs with 95% confidence intervals were considered as the effect size for all the included studies. ORs, RRs, or HRs were pooled with their 95% confidence intervals, with the assumption that these are comparable measures of association.

Additional outcome(s): None.

Data management: Records were managed by Endnote. Data were stored in Stata.

Quality assessment / Risk of bias analysis: Quality assessment was based on the Newcastle-Ottawa scale (NOS), as recommended by Cochrane Collaboration.

Strategy of data synthesis: ORs, RRs, or HRs were pooled with their 95% confidence intervals, with the assumption that these are comparable measures of association. The overall estimate of effect size was calculated based on a random-

effects model where any differences between studies were considered even if no statistically significant heterogeneity exists.

Subgroup analysis: Subgroup analysis will be performed by HCV or HBV infection.

Sensibility analysis: To test the robustness of meta-analytical results and to assess the excessive influence of individual studies on the pooled result, a sensitivity analysis was performed by sequentially omitting each study.

Language: English.

Country(ies) involved: China.

Keywords: Hepatic steatosis; hepatitis C virus; hepatic B virus, hepatocellular carcinoma; systematic review; meta-analysis.

Dissemination plans: None.

Contributions of each author:

Author 1 - Yan Xu - Yan Xu designed the study and contributed to writing.

Author 2 - Yuyang Zhao - Yuyang searched for databases.

Author 3 - Yong Wang - Yong Wang searched for databases.

Author 4 - Changyu Zhou - Changyu Zhou searched for databases.

Author 5 - Xingang Wang - Xingang Wang performed the selection of studies.

Author 6 - Yongqiang Dong - Xingang Wang performed the selection of studies.

Author 7 - Shaoyou Qin - Shaoyou Qin designed the study and contributed to writing and approved the last version.