Available online at www.sciencedirect.com

Public Health

journal homepage: www.elsevier.com/puhe

Review Paper

Hepatitis C and risk of coronary atherosclerosis – A systematic review

O.O. Olubamwo*, A.O. Aregbesola, J. Miettola, J. Kauhanen, T.-P. Tuomainen

Institute of Public Health and Clinical Nutrition, Faculty of Health Sciences, University of Eastern Finland, Kuopio, Finland

ARTICLE INFO

Article history:
Received 2 October 2015
Received in revised form
31 March 2016
Accepted 5 April 2016
Available online 18 May 2016

Keywords:
HCV
Coronary artery disease
Inflammation
Myocardial infarction
Meta-analysis

ABSTRACT

Background: Observational studies on the association of chronic hepatitis C with coronary atherosclerosis have shown varying results and previous related reviews have been inconclusive. By careful outcome classification and further data syntheses, we aimed to clarify current evidence on the association between hepatitis C infection and coronary atherosclerosis.

Methods: Through systematic searches of PubMed and Scopus, related published observational studies were identified. These were narrowed by review of abstract, full review and quality assessment to yield eligible studies. These were used in qualitative and quantitative syntheses.

Results: The initial search identified 274 unique publications, which were narrowed to 15 by means of preliminary reviews, and narrowed further to 10 by quality assessment. The endpoints assessed varied, representing different attributes of the disease. The 10 studies were used in the subsequent meta-analyses. The risk of a person with chronic hepatitis C developing coronary atherosclerosis is about triple the risk in uninfected persons (OR = 3.06, 95% CI = 1.99–4.72). Coronary atherosclerosis in persons with chronic hepatitis C is also more severe. The pooled risk of coronary atherosclerosis-related events in persons with chronic hepatitis C was null (OR = 1.10 95% CI = 0.80–1.52).

Conclusion: The current evidence indicates that hepatitis C virus or factors associated with HCV infection are apparently associated with increased risk of occurrence of coronary atherosclerosis and probably, increased severity of coronary atherosclerosis. Evidence of association with coronary atherosclerosis-related events is yet indeterminate.

* *Corresponding author*. Institute of Public Health and Clinical Nutrition, Faculty of Health Sciences, University of Eastern Finland, P.O. Box 1627, FI-70211 Kuopio, Finland.
E-mail address: olubunmi.olubamwo@uef.fi (O.O. Olubamwo).

http://dx.doi.org/10.1016/j.puhe.2016.04.005
0033-3506/

Introduction

Hepatitis C virus (HCV) infection is of global significance, with a global prevalence of 2–3%, and over 170 million persons chronically infected.[1,2] The virus causes acute or chronic necrotising inflammatory disease in the human liver but chronic infection has also been associated with extrahepatic manifestations including haematological, renal, endocrine and cardiovascular ones.[3] Cardiovascular manifestations that have been associated with HCV infection include coronary atherosclerosis and non-atherosclerotic coronary diseases such as cardiomyopathy and myocarditis.[4,5] Atherosclerosis is the most common cardiovascular disease, and a number of studies on the general population have showed that HCV markers are independently associated with coronary atherosclerosis, which is also called coronary artery disease.[6,7]

The estimated prevalence of coronary atherosclerosis in the general population is as high as 10 percent.[8] Despite the enormity of the burden of the disease, the aetio-pathogenesis is unresolved, and the occurrence of the disease process can only be linked to risk factors. Established risk factors include hyperlipidemic states, diabetes mellitus, smoking, hypertension and a positive family history.[9] However, the fact that these do not adequately explain the picture has stimulated continued search for more risk factors. More recently discovered risk factors include higher plasma concentrations of fibrinogen, hyperuricemia, homocysteinemia, C-reactive protein, lower plasma levels of adiponectin and chronic infection such as herpes and hepatitis C infection.[10,11] Hepatitis C infection stimulates production of pro-inflammatory cytokines, and is associated with insulin resistance and hepatic steatosis.[12] It is therefore speculated that chronic HCV infection has a potential for association with atherosclerosis.

There have been a number of epidemiological studies on the association of hepatitis C with coronary atherosclerosis.[13–16] These are observational as experimental studies in humans are ruled out due to ethical considerations.

Observational studies on the association of chronic HCV infection with atherosclerosis-related diseases have shown conflicting results. Some have reported no association between HCV infection and coronary atherosclerosis,[15,16] whereas others have reported an increased risk,[13,14] thereby necessitating systematic review of evidence. Karbasi-Afsha et al.[17] reviewed the contribution of hepatitis C virus infection to various cardiovascular diseases regardless of the pathological processes, and suggested that HCV has a significant effect on the development of coronary related cardiovascular diseases in the general population. Wong et al.[18] in their review on HCV and the risk of coronary artery disease, concluded that the association was unclear. Roed et al., in their evaluation of the literature on this association between chronic hepatitis C virus (HCV) infection and the risk of coronary artery disease (CAD), suggested an increased risk of CAD in HCV-infected individuals but did not synthesise the data obtained because of the heterogeneity in the included studies.[19] They concluded that further studies are needed to confirm their finding and also to evaluate the magnitude of the association.

However, a clarification of the association is necessary to guide clinicians regarding the reduction of CAD risk factors in patients with chronic HCV infection. This review focusses on coronary atherosclerosis-related outcomes in persons with chronic hepatitis C, considering the different coronary atherosclerosis outcomes separately and excludes studies of non-atherosclerosis-related cardiac outcomes of HCV infection. By excluding studies on subjects with potentially confounding co-morbidities or potentially confounding exposures or outcomes, careful grouping of studies with coronary atherosclerosis related outcomes and further syntheses of the data obtained, we explored the current body of evidence on the association of chronic hepatitis C with coronary atherosclerosis.

Methods

Search strategy

Published observational studies related to the topic were identified by systematic electronic searches of PubMed and Scopus online databases. The databases were searched on 18th January 2015. There was no restriction in language or date of publication. The search strategies incorporated hepatitis C and coronary atherosclerosis-related terms and text terms and these were adjusted to each database. A repeat search for new primary studies on the topic, done on 1st August 2015, revealed no new primary observational studies that addressed the topic. The references of relevant studies were also examined for additional studies. The search term used is shown in Table 1.

Study selection

In this study, we considered all analytical observational studies in which the subjects are diagnosed as having hepatitis C virus infection; all analytical observational studies in which the documented outcomes in subjects include clinical coronary atherosclerosis or coronary artery disease; and studies with the aforementioned exposure and outcome in which there was estimation of risk in the form of relative risk, odds ratio or hazard ratio. We excluded studies with documented multiple exposure in subjects, such as co-infection with hepatitis C virus and human immunodeficiency virus; studies in which multiple exposure types were considered together in the same study; studies on subjects with potentially confounding co-morbidities; and studies with exposure and outcome of interest without estimation of the risk. Table 2 shows the details of the inclusion and exclusion criteria. Articles were retrieved either through free internet access, University of Eastern Finland Nelli portal, purchase from journal through the university library or by kind donation from the corresponding authors.

Data extraction

Data extraction was carried out by two independent reviewers. Using a predesigned data extraction form, we extracted data on study characteristics. From each selected