

Letter to the Editor

Hepatitis C virus infection and atherosclerotic cardiovascular disease: recent knowledge, further insights

Dimitrios Ioannis Patoulas, Maria-Styliani Kalogirou

Second Propedeutic Department of Internal Medicine, General Hospital "Hippokration", Aristotle University of Thessaloniki, Thessaloniki, Greece

Address for correspondence

Dr. Dimitrios Ioannis Patoulas, Second Propedeutic Department of Internal Medicine, General Hospital "Hippokration", Aristotle University of Thessaloniki, Konstantinoupoleos 49, 54642, Thessaloniki, Greece, phone: 30-6946900777, fax: +30-2310225083, e-mail: dipatoulas@gmail.com

Dear Editor,

We have recently read with great interest the elegant paper authored by Piekarska *et al.* [1], who presented the results of the PRO-CARDIO-C study. The authors demonstrated in their large cohort that the relative frequency of positive anti-HCV (hepatitis C virus) antibodies and detectable HCV RNA in patients with coronary artery disease was not significantly different compared to that observed in patients hospitalized in a Dermatology Department (controls), despite the fact that the prevalence of chronic HCV infection was 5-fold higher compared to the general population [1].

Recently, Wen *et al.* published the results of their meta-analysis, demonstrating that HCV infection increases the risk of coronary artery disease (CAD) by 25% [risk ratio (RR): 1.25, 95% CI: 1.12-1.40] in cohort studies and the odds for CAD by 94% [odds ratio (OR): 1.58-2.38] in case-control and cross-sectional studies, establishing this close relationship [2]. Similar results were obtained by another meta-analysis in a total of 297,613 patients, confirming the association between HCV infection and cardio-cerebrovascular disease and its related mortality [3]. In a recent 13-year nationwide population-based study in Asia enrolling 31,943 patients either with chronic HBV (hepatitis B virus) or HCV infection it was shown that patients with HCV infection exhibit 38% greater risk of acute coronary syndrome (ACS) [hazard ratio (HR): 1.38, 95% CI: 1.02-1.85], compared to HCV patients, while they also exhibited a significant increase in the risk of all-cause mortality by 48%, acute ischemic stroke by 38% and composite arterial events (ACS, acute isch-

emic stroke, peripheral artery disease) by 29% [4]. However, data are contradictory concerning the angiographically proven atherosclerotic burden of CAD in patients with HCV infection compared to HCV negative control subjects [5, 6].

Thus, it seems undeniable that chronic HCV infection boosts the cardiovascular disease burden among the affected patients. The role of co-morbidities is of utmost importance, as it was recently observed in a US population-based study [7]. It would be interesting if Piekarska *et al.* could provide us with the patients' co-morbidities, mainly diabetes mellitus, chronic kidney disease, hypertension and obesity, as they might have an impact on their results [1]. Another recently published retrospective analysis demonstrated that the presence of hepatic steatosis in a large cohort of patients with chronic HCV infection increased almost 4-fold the risk of development of cardiovascular disease (HR: 5.2, 95% CI: 1.3-20.7), emphasizing the importance of timely and targeted counselling and multi-level assessment of these patients [8]. In the study by Piekarska *et al.*, 4 patients with chronic HCV infection and concomitant CAD exhibited hepatic fibrosis; however, no data on hepatic steatosis are provided [1]. Last, human immunodeficiency virus (HIV) infection also seems to be an additional burden for these patients; it has been shown in a recent meta-analysis that patients with HCV/HIV co-infection have a significant increase in the risk of cardiovascular disease by 24%, compared to those patients with HIV mono-infection [9]. No cases of HCV/HIV co-infection were reported in the cohort studied by Piekarska *et al.* [1].

Finally, we would like to comment on the impact of direct-acting antiviral (DAA) therapy. Current evidence suggests that treatment with a DAA regimen in chronic HCV patients is associated with a significant decrease in the risk of a cardiovascular event by 43% (HR: 0.57, 95% CI: 0.51-0.65), compared to no treatment [10]. DAA agents provide clear benefits for patients with chronic HCV infections, lowering overall cardiovascular risk. It would also be interesting if Piekarska *et al.* provide us with further results in the future, concerning the impact of the DAA regimen on CAD progression in their cohort.

In conclusion, the relationship between chronic HCV infection and cardiovascular disease seems to be undoubted. Assessment of the affected patient should be meticulous, with emphasis on co-morbidities and their multilevel therapeutic approach. DAA agents are really promising in terms of eliminating the cardiovascular disease burden among these patients.

Disclosure

The authors report no conflict of interest.

References

1. Piekarska A, Mamzer-Dachnowska A, Kasprzak J, et al. Prevalence of hepatitis C virus infection in patients hospitalised for ischemic heart disease versus controls – PRO-CARDIO-C study. *Clin Exp Hepatol* 2019; 5: 118-122.
2. Wen D, Du X, Dong JZ, Ma CS. Hepatitis C virus infection and risk of coronary artery disease: a meta-analysis. *Eur J Intern Med* 2019; 63: 69-73.
3. Ambrosino P, Lupoli R, Di Minno A, et al. The risk of coronary artery disease and cerebrovascular disease in patients with hepatitis C: A systematic review and meta-analysis. *Int J Cardiol* 2016; 221: 746-754.
4. Wu VC, Chen TH, Wu M, et al. Comparison of cardiovascular outcomes and all-cause mortality in patients with chronic hepatitis B and C: A 13-year nationwide population-based study in Asia. *Atherosclerosis* 2018; 269: 178-184.
5. Pothineni NV, Rochlani Y, Vallurupalli S, et al. Comparison of angiographic burden of coronary artery disease in patients with versus without hepatitis C infection. *Am J Cardiol* 2015; 116: 1041-1044.
6. Satapathy SK, Kim YJ, Kataria A, et al. Higher prevalence and more severe coronary artery disease in hepatitis C virus-infected patients: a case control study. *J Clin Exp Hepatol* 2013; 3: 186-191.
7. Asrani SK, Kouznetsova M, Ogola G, et al. Increasing health care burden of chronic liver disease compared with other chronic diseases, 2004-2013. *Gastroenterology* 2018; 155: 719-729.e4.
8. Rosso C, Caviglia GP, Ciruolo M, et al. Clinical outcomes in chronic hepatitis C long-term responders to pre-direct antiviral agents: a single center retrospective study. *Minerva Med* 2019; 110: 401-409.
9. Osibogun O, Ogunmoroti O, Michos ED, et al. HIV/HCV coinfection and the risk of cardiovascular disease: A meta-analysis. *J Viral Hepat* 2017; 24: 998-1004.
10. Butt AA, Yan P, Shuaib A, Abou-Samra AB, et al. Direct-acting antiviral therapy for HCV infection is associated with a reduced risk of cardiovascular disease events. *Gastroenterology* 2019; 156: 987-996.e8.