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ORIGINAL RESEARCH

Increased prevalence of coronary artery disease risk markers in patients with chronic hepatitis C – a cross-sectional study

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Objective: Chronic hepatitis C is a global health problem and has been associated with coronary artery disease. Our aim was to examine the prevalence of coronary artery disease risk markers including endothelial biomarkers in patients with chronic hepatitis C and matched comparisons without manifest cardiovascular disease or diabetes in a cross-sectional design.

Methods: Sixty patients with chronic hepatitis C (mean age 51 years) were recruited from the Department of Infectious Diseases at Copenhagen University Hospital, and compared with 60 age-matched non-hepatitis C virus-infected individuals from a general population survey. We examined traditional coronary artery disease risk factors, metabolic syndrome, carotid intima media thickness, and a range of endothelial biomarkers.

Results: Patients with chronic hepatitis C had more hypertension (40% versus 25%, prevalence ratio [PR] 1.6; 95% confidence interval [CI] 0.9–2.7) and smoked more (53% versus 38%, PR 1.4; 95% CI 0.9–2.1). The two groups had similar body mass index (mean 25.0 versus 25.7 kg/m^2), whereas those with chronic hepatitis C had less dyslipidemia (including significantly lower low-density lipoprotein and cholesterol/high-density lipoprotein ratio), higher glycosylated hemoglobin level (mean 6.2 versus 5.7, difference of means 0.5; 95% CI 0.3–0.8), and a higher prevalence of metabolic syndrome (28% versus 18%, PR 1.6; 95% CI 0.8–3.0). Increased carotid intima media thickness above the standard 75th percentile was seen more frequently in chronic hepatitis C (9% versus 3%, PR 1.7; 95% CI 0.4–6.7), though difference of means was only 0.04 mm (95% CI 0.00–0.10). Patients with chronic hepatitis C had increased hsCRP (high-sensitivity C-reactive protein), sICAM-1 (soluble intercellular adhesion molecule-1), sVCAM-1 (soluble vascular cell adhesion molecule-1), and soluble E-selectin, but lower levels of tPAI-1 (tissue-type plasminogen activator inhibitor-1), MMP9 (matrix metallopeptidase 9), and MPO (myeloperoxidase) than their comparisons.

Conclusion: Our findings indicate that patients with chronic hepatitis C have increased prevalence of several coronary artery disease risk markers. These results may be important when evaluating the appropriateness of screening for coronary artery disease and its risk factors in chronic hepatitis C.

Keywords: risk factors, atherosclerosis, endothelial dysfunction, biomarkers, metabolic syndrome, intima media thickness

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Introduction

Chronic hepatitis C (CHC) is a global health problem, with an estimated 180 million people infected worldwide.[1] The population prevalence in Denmark is estimated to be 0.4%.[2] CHC and other chronic infections such as *Chlamydophila pneumoniae*, herpes simplex virus, and human immunodeficiency virus (HIV), have been associated with increased risk for developing coronary artery disease (CAD).[3]

The evidence for a causal association between CHC and CAD remains conflicting. A recent systematic review found that among the studies of the highest quality, five out of six studies found odds ratio (OR) estimates above 1 for this association, ranging from 1.27 to 5.71.[4] For example, an American historical follow-up study of 82,000 veterans with CHC and 89,600 healthy controls found increased risk of CAD in patients with CHC, with a hazard ratio of 1.27 (95% confidence interval [CI] 1.22–1.31), controlling for known CAD risk factors at baseline.[5] However, another study, using a historical cohort design to examine medical and psychiatric comorbidities among American veterans with CHC, found a negative association between CHC and CAD, with an adjusted OR of 0.74 (95% CI 0.71–0.76) for CAD in CHC patients.[6] Several biological mechanisms have been proposed to explain a relation between CHC and CAD. Hepatitis C virus (HCV)-ribonucleic acid (RNA) has been demonstrated in carotid plaques,[7] and CHC infection may be associated with increased foam-cell development, induction of autoimmune reactions, activation of pro-coagulants, and induction of changes in lipoproteins.[3]

There are sparse data on the prevalence of different CAD risk markers in patients with CHC. The presence of metabolic syndrome (MS) is known to increase the risk of both CAD and type 2 diabetes mellitus two to three times,[8] and MS seems to be highly prevalent (ie, 25%–61%) in CHC patients in different settings,[9–12] but data from studies with control groups are few. The ultrasonographically measured carotid intima media thickness (CIMT) predicts CAD and stroke in healthy patients,[13] but the few studies on CIMT in CHC patients are conflicting. Ishizaka et al found that HCV seropositivity was associated with increased CIMT and carotid plaque,[14] whereas Kiechl et al found no association between carotid plaque and chronic viral hepatitis.[15] Several biomarkers of endothelial inflammation and dysfunction have been used in studies of atherosclerosis, but these markers, to our knowledge, have never been studied in CHC patients. Biomarkers that may predict CAD include high-sensitivity C-reactive protein (hsCRP), soluble vascular cell adhesion molecule-1 (sVCAM-1), soluble intercellular adhesion molecule-1 (sICAM-1), soluble E-selectin (s-E-selectin), tissue-type plasminogen activator inhibitor-1 (tPAI-1), matrix metallopeptidase 9 (MMP9), and myeloperoxidase (MPO).[16–29]

Knowledge about risk factors for developing CAD and atherosclerotic mechanisms in patients with CHC is crucial to understand their risk of future CAD, and thus to evaluate the possible effect of future screening and intervention against CAD risk factors. Our aim was therefore to undertake a cross-sectional study of CHC patients and an age-matched comparison group without known manifest cardiovascular disease or diabetes to comprehensively examine the prevalence of traditional CAD risk factors, MS, CIMT, as well as a range of endothelial biomarkers.

Materials and methods

Study population of CHC patients and comparison group

We consecutively recruited 60 patients with CHC, between December 2010 and July 2011, from the hospital specialist outpatient clinic at the Department of Infectious Diseases, Copenhagen University Hospital, Hvidovre, Denmark. Inclusion criterion was a prevalent infection with confirmed CHC, defined as two positive HCV-RNA-tests measured 6 months apart. Patients were aged between 18 and 70 years, with the ability to understand and give informed consent. None of the patients with CHC had undergone antiviral therapy for at least 1 year prior to inclusion. Exclusion criteria were diagnosis of diabetes mellitus, ischemic heart disease, or decompensated heart disease, a prior cardiovascular event, co-infection with HIV or hepatitis B virus, pregnancy, and lactation.

Power calculations, using the methods described by Kirkwood and Sterne,[30] were done in advance, showing 60 HCV-infected patients and 60 comparisons were sufficient.

The patients with CHC were compared with 60 HCV-uninfected individuals without known cardiovascular disease or diabetes, matched on age (10-year age groups). The comparison group was recruited randomly among individuals in a larger control group (n=100) from a study of cardiovascular risk factors in HIV patients and controls (Kristoffersen US, unpublished data, 2012). These were then drafted into the current study since identical inclusion and exclusion criteria and similar outcomes were measured. This allowed for matching on age, but not sex. The comparison group was originally recruited randomly from participants in The Copenhagen City Heart Study,[31] a well established cohort of general population members, using questionnaires followed up by clinical examination as described below.

Ethics statement

Written informed consent was obtained from each individual participating in the study. The regional Danish Scientific Ethical Committee (journal number H-3-2010-081) and the Danish Data Protection Agency (journal number 2010-41-5028) approved the study.

Data collection on CAD risk markers

Data on the 60 patients with CHC and the 60 HCV-uninfected individuals were collected at the clinical examination, which took place in a quiet, temperature- and brightness-controlled room. A detailed medical history was obtained along with demographic and anthropometric variables, including smoking status, body mass index (BMI), and waist width. CIMT and blood pressure were measured after 5 minutes in the supine position.

The CIMT was visualized in the common carotid artery, 1 cm caudally to the carotid bulb by ultrasonography, with a SonoSite M-turbo (SonoSite, Bothell, WA, USA), using a 13.6 MHz linear transducer. A recording of the vessel seen in longitudinal view was made with both the near and far wall visible. The CIMT was computed as the mean value of the far wall on both sides using Carotid Analyzer for Research, version 5.7.3 (Medical Imaging Applications LCC, Coralville, IA, USA). A valid measurement was obtainable in 58 of 60 CHC patients, and in all 60 HCV-uninfected individuals.

Blood samples were drawn at the end of the examination and then brought immediately for analysis. The blood samples used for examining endothelial biomarkers were drawn into EDTA (ethylenediaminetetraacetic acid)-coated Vacuette tubes (Greiner Bio-One, Kremsmünster, Austria), pre-added with 5,000 IU of aprotinin, separated by centrifuge, and then plasma was frozen at –80°C.

MPO, hsCRP, s-E-selectin, sVCAM-1, sICAM-1, MMP9, and tPAI-1 were measured using high sensitivity Luminex multiplex assays (Luminex Corporation, Austin, TX, USA) according to the manufacturer's instructions. In our laboratory the lower limit of quantification was 4 ng/mL for s-E-selectin, sVCAM-1, and sICAM-1, and 0.8 ng/mL for MMP9, MPO, tPAI-1, and hsCRP. All measurements were performed in duplicate, with the mean being used. The accepted threshold of the coefficient of variation was 20%. Two measurements of tPAI-1 and one of hsCRP were above this, and were therefore excluded pairwise in the analyses of tPAI-1 and hsCRP.

Transient elastography was used to evaluate liver damage (Fibroscan, model 502; Echosens, Paris, France). If records less than 48 months old were unavailable, a new scan was performed. The median value of at least ten measurements was used, and the result discarded if the interquartile range exceeded 25% of the median value. A valid fibroscan was obtained in 57 of the 60 CHC patients.

Definitions

Hypertension was defined as systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg, or current use of antihypertensive drugs.

We defined MS as presence of waist width ≥94 cm in men and ≥80 cm in women or a BMI ≥30, combined with at least two of the following: triglyceride level ≥1.7 mmol/L or antidyslipidemic treatment (including statins); reduced high density lipoprotein (HDL) (<1.0 mmol/L in males, <1.3 mmol/L in females); systolic blood pressure ≥130 mmHg, diastolic blood pressure ≥85 mmHg, or antihypertensive treatment; and/or fasting glucose ≥5.6 mmol/L.[8] These criteria were used since National Cholesterol Education Program criteria are known to underestimate MS prevalence.[32]

The American Society of Echocardiography and the Society for Vascular Medicine recommends reporting CIMT as both mean thickness with CIs and as increased CIMT. The latter is defined as an age- and sex-dependent value above the 75th percentile of a comparable population, as values in the 25th–75th percentile range are considered average, and indicative of unchanged CVD risk.[33] We determined the threshold CIMT value in each individual using age- and sex-stratified data derived from a large German population-based study, to define increased CIMT. Threshold values (in millimeters) in males ranged from 0.585 (35 years) to 1.028 (75 years) and in women from 0.575 (35 years) to 0.921 (75 years).[33,34]

The ideal cutoff point for increased hsCRP, in terms of cardiovascular disease risk, is not agreed upon. One, which is commonly used, and which has been proposed for initiation of statin therapy,[35] is 2.0 mg/mL.

Statistical methods

We compared the prevalence of categorical traditional CAD risk factors (sex, smoking status, and hypertension), the MS, increased hsCRP and increased CIMT (defined as described above) in CHC patients and comparisons, and calculated prevalence proportion ratios (PR) with 95% CIs, as an estimation of the relative risk. We examined the means of continuous traditional CAD risk factors (age, BMI, waist width, lipid status, creatinine, fasting glucose, and glycosylated hemoglobin [HbA_{1c}] level) along with CIMT in millimeters and biomarkers in patients with CHC and comparisons, and calculated difference of means with 95% CIs. Correlations were calculated as Pearson's correlation. Analyses were performed using PASW 19 (SPSS) (IBM Corporation, Armonk, NY, USA).

Results

Baseline characteristics and traditional cardiovascular risk factors

Demographic variables and traditional cardiovascular risk factors measured in patients with CHC and matched comparisons are outlined in Table 1.

Table 1 Baseline characteristics and traditional cardiovascular risk factors among 60 CHC patients and 60 matched HCV-uninfected controls

	CHC patients	HCV-uninfected	PR (95% CI)
	Count (%)	Count (%)	
Sex (% male)	37 (61.7)	53 (88.3)	0.69 (0.56–0.87)
Smoking status			
Current	32 (53.3)	23 (38.3)	1.39 (0.93–2.07)
Former	17 (28.3)	12 (20.0)	1.41 (0.74–2.70)
Non-smoking	11 (18.3)	25 (41.7)	0.44 (0.24–0.81)
Arterial hypertension (%)	24 (40.0)	15 (25.0)	1.60 (0.94–2.74)
HCV genotype			
1	33 (55.9)	–	–
2	9 (15.3)	–	–
3	17 (28.8)	–	–
	Mean (SD)	Mean (SD)	Difference of means (95% CI)
Age (years)	50.8 (8.6)	49.5 (7.9)	1.32 (–1.63–4.28)
Body mass index (kg/m^2)	25.0 (4.7)	25.7 (3.1)	–0.62 (–2.03–0.80)
Waist width (cm)	91.4 (14.3)	92.0 (11.1)	–0.62 (–5.73–4.49)
Cholesterol (mmol/L)			
Total cholesterol	4.4 (1.0)	5.2 (0.9)	–0.80 (–1.15 to –0.45)
LDL	2.5 (0.7)	3.3 (0.9)	–0.80 (–1.09 to –0.51)
HDL	1.5 (0.7)	1.4 (0.4)	0.12 (–0.08–0.31)
Triglyceride	0.9 (0.3)	1.2 (0.7)	–0.27 (–0.46 to –0.07)
Cholesterol/HDL-ratio	3.3 (1.0)	4.1 (1.3)	–0.82 (–1.24 to –0.39)
Creatinine (μmol/L)	68.4 (14.7)	75.1 (9.1)	–6.69 (–11.32 to –2.07)
Fasting glucose (mmol/L)	5.5 (0.6)	5.4 (1.3)	0.12 (–0.24–0.47)
Hemoglobin A_{1c} (%)	6.2 (0.8)	5.7 (0.7)	0.53 (0.27–0.80)

Abbreviations: CHC, chronic hepatitis C; CI, confidence interval; HCV, hepatitis C virus; PR, prevalence ratio; SD, standard deviation; LDL, low density lipoprotein; HDL, high density lipoprotein.

The majority of the patients with CHC were infected with HCV genotype 1 (56%) or genotype 3 (29%). Fibroscan revealed a tendency toward liver damage in the CHC patients, with a median of 6.8 kPa. Twenty-seven patients with CHC (47.3%) had a fibroscan value >7 kPa, requiring further examination, and seven patients (12.3%) had a fibroscan value >17 kPa, the cutoff score used in Danish national guidelines to signify cirrhosis at that time point.[2]

Patients with CHC were less likely to be male than their comparisons (62% versus 88%, PR 0.7; 95% CI 0.6–0.9), and they had a higher prevalence of current smoking (53% versus 38%, PR 1.4; 95% CI 0.9–2.1). CHC patients also had more hypertension (40% versus 25%, PR 1.6; 95% CI 0.9–2.7), a similar waist width and BMI (mean 25.0 versus 25.7 kg/m^2), a more favorable lipid profile with a lower cholesterol/HDL ratio (difference of means –0.82; 95% CI –1.24 to –0.39), yet a higher HbA_{1c} level (mean 6.2 versus 5.7, difference of means 0.5; 95% CI 0.3–0.8).

Other cardiovascular risk markers

The other measured risk markers are presented in Table 2. Patients with CHC had a higher prevalence of MS (28% versus 18%, PR 1.6; 95% CI 0.8–3.0).

The difference in mean CIMT between patients and the comparison group was 0.04 mm (95% CI 0.00–0.08), and more patients had an increased CIMT above the standard population 75th percentile (9% versus 3%, PR 1.7; 95% CI 0.4–6.7).

The mean level of the endothelial biomarker hsCRP was twice as high among patients with CHC as in the comparison group, and the PR of having increased hsCRP above 2.0 ng/mL was 1.2 (95% CI 0.8–1.7). Patients with CHC had

Table 2 Cardiovascular risk markers among 60 CHC patients and 60 matched HCV-uninfected controls

	CHC patients	HCV-uninfected	PR (95% CI)
	Count (%)	Count (%)	
Increased CIMT[a]	5 (8.6)	2 (3.3)	1.67 (0.42–6.66)
Increased hsCRP (>2 mg/mL)	32 (53.3)	27 (45.0)	1.19 (0.82–1.71)
Metabolic syndrome	17 (28.3)	11 (18.3)	1.55 (0.79–3.02)
	Mean (SD)	Mean (SD)	Difference of means (95% CI)
CIMT (mm)	0.66 (0.11)	0.62 (0.11)	0.04 (0.00–0.08)
hsCRP (mg/mL)	7.15 (16.2)	3.74 (5.1)	3.41 (–0.98–7.80)
sICAM-1 (ng/mL)	248.3 (137.3)	125.5 (47.7)	122.87 (85.53–160.20)
sVCAM-1 (ng/mL)	1440.8 (509.0)	1103.6 (180.1)	337.20 (198.5–475.89)
s-E-selectin (ng/mL)	65.6 (41.8)	23.4 (13.9)	42.25 (30.93–53.58)
tPAI-1 (ng/mL)	57.3 (31.2)	72.8 (37.6)	–15.52 (–27.98 to –3.06)
MMP9 (ng/mL)	65.4 (46.8)	91.2 (46.7)	–25.82 (–42.70 to –8.94)
MPO (ng/mL)	41.1 (99.5)	94.0 (129.0)	–52.83 (–94.32 to –11.34)

Note: [a]Age- and sex-dependent, see text for explanation.
Abbreviations: CHC, chronic hepatitis C; CIMT, carotid intima media thickness; HCV, hepatitis C virus; hsCRP, high-sensitivity C-reactive protein; MMP9, matrix-metallopeptidase 9; MPO, myeloperoxidase; PR, prevalence ratio; SD, standard deviation; s-E-selectin, soluble E-selectin; sICAM-1, soluble intercellular adhesion molecule 1; sVCAM-1, soluble vascular adhesion molecule 1; tPAI-1, tissue-type plasminogen activator inhibitor; CI, confidence interval.

higher levels of sICAM-1, sVCAM-1, and s-E-selectin, but lower levels of tPAI-1, MMP9, and MPO.

The endothelial biomarker measurements in our laboratory had high reproducibility, with mean coefficients of variation as follows: hsCRP 5.1%, sICAM-1 4.7%, sVCAM-1 5.0%, s-E-selectin 4.6%, tPAI-1 8.7%, MMP9 3.8% and MPO 6.9%.

The correlation between MS, CIMT, and endothelial biomarker levels ranged from r=–0.16 (between E-selectin and MMP9) to r=0.45 (between MPO and MMP9). CIMT and MS correlated poorly, with r=0.08. The only correlation to reach statistical significance, was that between tPAI-1 and MS, with r=0.203.

Discussion

In the present study, we found a range of cardiovascular risk markers to be more prevalent in patients with CHC compared with non-HCV infected individuals of similar age.

More patients with CHC had increased CIMT than in the comparison group. Having increased CIMT above the 75th percentile of a comparable population has been associated with increased risk of myocardial infarction in several studies, including a cohort study from Holland (n=6,389), where the relative risk for myocardial infarction was 1.95 (95% CI 1.19–3.19).[36] However, the absolute risk of such CIMT elevation was small in our study, and it remains unclear whether the small absolute difference in mean CIMT that we observed is clinically relevant.

Patients with CHC had a higher risk of having MS, in spite of an advantageous lipid profile and the exclusion of patients with overt diabetes. It was predominantly caused by the higher prevalence of hypertension and higher fasting glucose in the patients with CHC, since BMI and waist width did not differ significantly between the two groups. Along with the increased HbA_{1c} level, this indicates increased insulin resistance in patients with CHC.

The majority of endothelial biomarkers were elevated in the CHC patients. Although varied, the biomarker pattern points to an increased risk of cardiovascular mortality in the CHC patients: CRP, sVCAM-1, sICAM-1, and s-E-selectin, which were all elevated in the patients as compared with comparisons, have been shown to be associated with subsequent risk of acute coronary syndrome and cardiovascular mortality in several follow-up studies.[16,18–20,22,23] Collet et al have also shown this association for tPAI-1,[24] but found that it disappeared when adjusting for insulin resistance. tPAI-1 was elevated in our comparison group, making it difficult to draw conclusions. Also elevated in the comparison group, MPO has been shown to be associated with CAD development in one case-control study,[25] and MPO and MMP9 have been shown to predict increased severity of cardiac events during follow-up (eg, acute coronary syndrome instead of stable angina episodes) in patients with known CAD.[27–29] How to quantitatively translate biomarker increase into CAD risk increase remains undetermined.

A recent study on a range of endothelial biomarkers, including s-E-selectin and sICAM-1, in HIV/HCV-coinfected individuals found that elimination of the HCV-virus caused the biomarkers to decrease.[37] Whether this would be the case for all the biomarkers examined in this study remains unknown, as does the question of whether the biomarker level decrease reflects a change in future risk of CAD.

Patients with liver cirrhosis have been shown to have lower incidence of CAD,[38,39] probably because of the coagulation abnormalities, thrombocytopenia, low cholesterol, and low blood pressure observed in cirrhotics. Of the CHC patients, 12% had fibroscan scores clearly signifying severe fibrosis/cirrhosis, but the fibroscan score correlated poorly with the risk markers, making it less likely that our results are affected by this (data not shown).

The strength of this study is that, to our knowledge, it is the first to evaluate comprehensive cardiovascular risk markers including biomarkers in patients with CHC while comparing them to a matched non-HCV-infected population. Our study used repeated measurements of HCV-RNA to establish the chronicity of HCV infection, something that only few studies have done.[4]

There are, however, several limitations to this study. First, the limited sample size led to low statistical precision of the prevalence ratio estimates, and hampered our ability to adjust for potential confounding factors. For example, it would be important to adjust for the risk posed by the increased prevalence of smoking, as this could account for some of the differences seen between the two groups. Second, we did not have available data on previous drug abuse, socioeconomic status, or family history of CAD. These are strong CAD risk factors on their own and could be associated with CHC.[40] Indeed, one study found that patients with CHC in Denmark have a much higher prevalence of drug and alcohol abuse than the general population (48% versus 1% and 11% versus 1%, respectively).[41] Third, the cross-sectional nature of our study did not allow us to disentangle the exact time order and collinearity for several risk markers. For example, MS and insulin resistance may lead to subsequent increased CIMT and possibly to increased endothelial biomarker levels as well, but the low degree of correlation between these risk markers suggests this is not the case. Nonetheless, the individual factors may

still be valuable markers of increased cardiovascular risk. Finally, the fact that we were unable to match the two groups on sex means that this could account for some of our results. However, given that males have an increased risk of CAD, it is possible that the observed increase in CAD risk in HCV-infected patients is in fact an underestimation.

Our findings are in line with several other studies. Huang et al reported a prevalence of 25% for MS in patients with CHC in Taiwan and 13% in healthy individuals,[11] and Hanouneh et al reported MS in 26% of patients with CHC in the USA.[9] These figures are similar to our finding of MS in 28% of our CHC patients. Grigorescu et al reported prevalence as high as 61% in patients with CHC in Romania.[10] This is important, since the presence of MS has been shown to be associated not only with CAD and type 2 diabetes mellitus, but also with poorer response to antiviral treatment and more rapid progression of liver fibrosis.[42,43]

The association between CIMT and CHC is still controversial. Our findings confirm the results found by Ishizaka et al, who found an OR of 1.9 (95% CI 1.6–2.4) for CIMT increase (defined as >1.0 mm) in patients with CHC,[14] compared with the 1.7 times increased risk of having CIMT increased above the 75th percentile found by us, though our threshold was lower. Kiechl et al found no association between carotid artery plaque or chronic viral hepatitis,[15] while Bilora et al found CHC to be a plaque protective factor, finding carotid artery plaque in 27% of CHC patients and in 56% of controls ($P<0.005$).[44]

It is interesting that the above findings were in spite of an advantageous lipid profile. These findings confirm the results from Corey et al, who also noted low lipids in patients with CHC, speculating it is because of the dependency of the HCV replication on the lipid assembly apparatus.[45] The reason that CIMT might be increased in patients with CHC may include the local action of HCV-RNA in the vessel walls and increased foam-cell development.[3,7]

Our study is the first to examine these endothelial biomarkers in patients with CHC, which in many studies have shown their predictive capabilities in non-infected individuals.[16–29] A number of these biomarkers are so far only useful in research due to their unclarified role in CAD risk prediction and their high cost.

Several studies have indicated an association between CAD and CHC, as described above, and the clear elevation of several circulating endothelial biomarkers in the present study suggests that this could be on the basis of an increased systemic inflammation due to chronic infection. However, it also seems likely that lifestyle and socioeconomic issues play an important role. This association is not well understood, and it is unclear whether the infection is causally linked to CAD or whether the association is driven by socioeconomic and lifestyle factors.

In conclusion, although our findings were conflicting, they indicate that CHC virus infection may be associated with increased prevalence of CAD risk factors compared with non-HCV-infected individuals. It is therefore of importance that clinicians caring for patients with CHC are aware of those risk factors that are potentially modifiable. This is relevant whether the association is causally linked to the infection or not. It is particularly important in regard to MS, since it may affect CHC treatment response and the clinical course of the infection. Further research needs to be done, both to examine the magnitude of the risk of manifest CAD in patients with CHC, but also to clarify the question of how, and when, to evaluate and treat CAD risk factors in patients with CHC.

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Disclosure

The authors report no conflicts of interest in this work.

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