Journal of Geriatric Cardiology (2014) 11: 192−199

Research Article · **Open Access** ·

Relationship between lipids levels and right ventricular volume overload in congestive heart failure

Ying CHEN[1*], Xiao-Mei HE[2*], Hong MENG[2], Qing-Zhen ZHAO[2], Yu-Zhi ZHEN[2], Li TIAN[2], Le WANG[2], Li-Shuang JI[2], Guo-Ping MA[2], Yu TIAN[2], Gang LIU [2], Zhen-Guo JI[2], Kun-Shen LIU [2], Chao LIU[2]

[1]*Emergency Department, First Hospital of Hebei Medical University, Hebei Medical University, No. 89 Donggang Road, Shijiazhuang 050032, Hebei Province, China*

[2]*Heart Center, First Hospital of Hebei Medical University, Hebei Medical University, No. 89 Donggang Road, Shijiazhuang 050032, Hebei Province, China*

Abstract

Background The relationship between lipids and coronary artery disease has been well established. However, this is not the case between lipids and heart failure. Ironically, high lipid levels are associated with better outcomes in heart failure, but the mechanisms underlying the phenomenon are not fully understood. This study was performed to test the hypothesis that reduced intestinal lipid absorption due to venous congestion may lead to low lipid levels. **Methods** We collected data of clinical characteristics, echocardiograph, and lipid profile in 442 unselected patients with congestive heart failure. Correlations between lipid levels [including total cholesterol (TCL), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG)] and right ventricle end diastolic diameter (RVEDD), left ventricle end diastolic diameter (LVEDD), right atrium diameter (RA), left atrium diameter (LA), or left ventricle ejection fraction (LVEF) were analyzed using Pearson correlation and partial correlation. RVEDD, LVEDD, RA, and LA were indexed to the body surface area. **Results** There was a significantly inverse correlation between TCL levels and RVEDD ($r = -0.34$, $P < 0.001$) and RA ($r = -0.36$, $P < 0.001$). Other lipids such as LDL-C, HDL-C, and TG had a similar inverse correlation with RVEDD and RA. All these correlations remained unchanged after adjusting for age, gender, smoking status, physical activity levels, comorbidities, and medication use. **Conclusions** Lipid levels were inversely correlated to RVEDD in patients with congestive heart failure; however, because this was an observational study, further investigation is needed to verify our results as well as identify a causal relationship, if any.

J Geriatr Cardiol 2014; 11: 192−199. doi:10.11909/j.issn.1671-5411.2014.03.011

Keywords: Lipid levels; Heart failure; Right ventricle; Volume overload; Correlation analysis

1 Introduction

Congestive heart failure (CHF) is a clinical syndrome marked by venous congestion and maladaptive neurohormonal activation in the setting of left ventricular dysfunction.[1] Recent evidence has shown the occurrence of lipid metabolic derangements in this syndrome.[2,3] The relationship between lipids and coronary artery disease, both from pathogenesis to risk determination and from treatment to clinical outcomes, is well established.[4] However, this is not the case between lipids and CHF. Hyperlipidemia is associated with a higher risk of development of CHF.[5–7] Ironically, newly emerging evidence from randomized clinical trials has shown that lipid lowering therapy does not reduce mortality in CHF;[8–10] instead, high cholesterol levels are associated with better outcomes in CHF.[11–13] This phenomenon is defined as an epidemiologic paradox, and its underlying mechanisms are not fully understood.[3]

Venous congestion, due to volume overload can worsen renal function and impair glomerular filtration in CHF.[14,15] Venous congestion in CHF also impairs absorption of water, electrolytes, and glucose. We hypothesized that venous congestion in CHF may lead to low lipid

*The first two authors contributed equally to the work.

Correspondence to: Chao LIU, MD, Associate Professor, Heart Center, The First Hospital of Hebei Medical University, No. 89 Donggang Road, Shijiazhuang, Hebei 050032, China. E-mail: dr.liuchao@gmail.com

Telephone: + 86-311-85917032 **Fax:** +86-311-85917290

Received: February 26, 2014 **Revised:** August 14, 2014

Accepted: August 20, 2014 **Published online:** September 19, 2014

levels in CHF due to reduced lipid absorption. Therefore, we analyzed the relationship between lipid levels and right ventricle end diastolic diameter (RVEDD), which is a good indicator of the chronic volume overload status in CHF.

2 Methods

This cross-sectional study was approved by the institutional ethics committee and conducted in adherence with local guidelines for good clinical practice. We reviewed the medical records of 442 patients with CHF who were treated in our heart center between January 2005 and March 2010. The diagnosis of CHF was based on clinical symptoms and a combination of clinical signs and echocardiogram. The exclusion criteria were familial hypercholesterolemia, familial hyper-triglyceridemia, terminal illness, chronic liver disease, cachexia, acute myocarditis, acute coronary syndrome, pregnancy, renal function insufficiency [serum creatinine (SCr) < 200 μmol/L], nursing mothers, and sepsis. Patients were also excluded from the analysis when variables (i.e., lipid profile and echocardiographic data) were not available from the same time point (defined as a maximum interval of 7 days). The detailed clinical characteristics and medications are listed in Table 1.

2.1 Laboratory assays

Blood samples for lipid level analysis were taken in the morning, and total cholesterol (TCL), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG) levels were directly measured with a UNICEL DxC 800 (Beckman Coulter, USA) automatic analyzer system immediately after blood samples were obtained. For quality control, during operation of the Beckman Coulter AU analyzer, at least two levels of lipid control material were tested (a minimum of once a day).

2.2 Echocardiographic measurements

All chamber measurements were performed according to guidelines and recommendations by the European Association of Echocardiography.[16] The diameter of left atrium (LA) was measured from M-mode, guided by a parasternal long-axis image at the level of the aortic valve. Left ventricle end diastolic diameter (LVEDD was measured from M-mode, guided by parasternal long-axis image at the level of the tip of the mitral valve. Diameter of right atrium (RA) was measured along the minor-axis that was perpendicular to the long axis of RA and extended from the lateral border of RA to the inter-atrial septum in the

Table 1. Clinical characteristics of patients with congestive heart failure (*n* = 442).

Variables	Value
Age, yrs	61.92 ±14.78
Female	223 (40.33%)
BMI, kg/m^2	25.12 ±3.74
MI	100 (22.6%)
IDC	88 (19.9%)
VHD	75 (17.0%)
HTN	70 (15.8%)
AF	136 (30.7%)
DM	85 (19.2%)
NYHA functional class	
I	40 (9.0%)
II	92 (20.8%)
III	139 (31.4%)
IV	171 (38.7%)
Echocardiographic data	
LA, cm	45.08 ±10.39
LA/BSA, cm/m^2	23.19 ±5.76
RVEDD, cm	37.76 ±8.89
RVEDD/BSA, cm/m^2	19.47 ±5.08
RA, cm	41.43 ±11.51
RA/BSA, cm/m^2	21.37 ±6.47
LVEDD, cm	55.62 ±13.84
LVEDD/BSA, cm/m^2	28.51 ±7.26
LVEF	47.33% ±16.38%
Laboratory test	
FG, mmol/L	6.06 ±2.68 (NR: 3.9–6.1)
TCL, mmol/L	4.23 ±1.24 (NR < 5.17)
TG, mmol/L	1.37 ±0.98 (NR: 0.20–1.70)
LDL-C, mmol/L	2.55 ±1.04 (NR < 3.20)
HDL-C, mmol/L	1.07 ±0.49 (NR 0.80–1.80)
Medications	
Furosemide	252 (57.0%)
HCTZ	231 (52.38%)
Furosemide and HCTZ	125 (28.3%)
Spironolactone	36.9 (83.5%)
Digitalis	185 (41.9%)
ACEI	265 (60.0%)
ARB	64 (14.5%)
CCB	76 (17.2%)
β-blocker	339 (61.30%)
Warfarin	89 (20.1%)
Statin	158 (35.7%)

Data are expressed as mean ± SD or *n* (%). ACEI: angiotensin-converting enzyme inhibitors; AF: atrial fibrillation/flutter; ARB: angiotensin II receptor blockers; BMI: body mass index; BSA: body surface area; CCB: calcium channel blocker; DM: diabetes mellitus; FG: fasting glucose; HCTZ: hydrochlorothiazide; HDL-C: high-density lipoprotein cholesterol; HTN: hypertension; IDC: idiopathic dilated cardiomyopathy; LA: left atrium; LDL-C: low-density lipoprotein cholesterol; LVEDD: left ventricle end diastolic diameter; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NR: normal range; NYHA: New York Heart Association; RA: right atrium; RVEDD: right ventricle end diastolic diameter; TCL: total cholesterol; TG: triglyceride; VHD: valvular heart disease.

apical four-chamber view. Right ventricle end diastolic diameter (RVEDD) was measured along the minor-axis in the apical four-chamber view, at a level which was approximately one-third from the base of the ventricle.

2.3 Statistical analysis

Statistical analysis were carried out using SPSS 16.0 statistical package. The Pearson correlation coefficients were derived. Variables, such as LA, LVEDD, RA, RVEDD, and left ventricular ejection fraction (LVEF) were indexed to the body surface area (BSA). Correlation coefficients were also calculated in subgroups stratified by LVEF (i.e., patient with preserved LVEF and patients with systolic heart failure) and statin treatment (i.e., patients on statin treatment and those not on statin treatment). We also conducted partial correlation using the following as co-variables to rule out any potential bias: age, gender, smoking status, physical activity levels, comorbidities (myocardial infarction, atrial fibrillation/flutter, diabetes mellitus, idiopathic dilated cardiomyopathy, valvular heart disease, and hypertension), and medication use. A multiple linear regression was used to model the dependence of lipid levels on age, gender, statin therapy, and echocardiographic parameters. Standardized coefficients were calculated to reflect the relationship between lipid levels and echocardiographic parameters.

3 Results

3.1 Relationship between lipid profile and echocardiographic data in patients with CHF

The univariate correlation coefficients between variables of patients with CHF are shown in Figure 1. The analysis using Pearson's correlation coefficient indicated that there was a statistically significant linear inverse relationship between concentrations of TCL and RVEDD (r = –0.34, P < 0.0001, Figure 1). The strongest correlation was observed between concentrations of TCL with RVEDD and RA (r = –0.36, P < 0.0001, Figure 1). There was a similar but weaker correlation of concentrations of LDL-C, LDL-C, and TG with RVEDD and RA (Table 2).

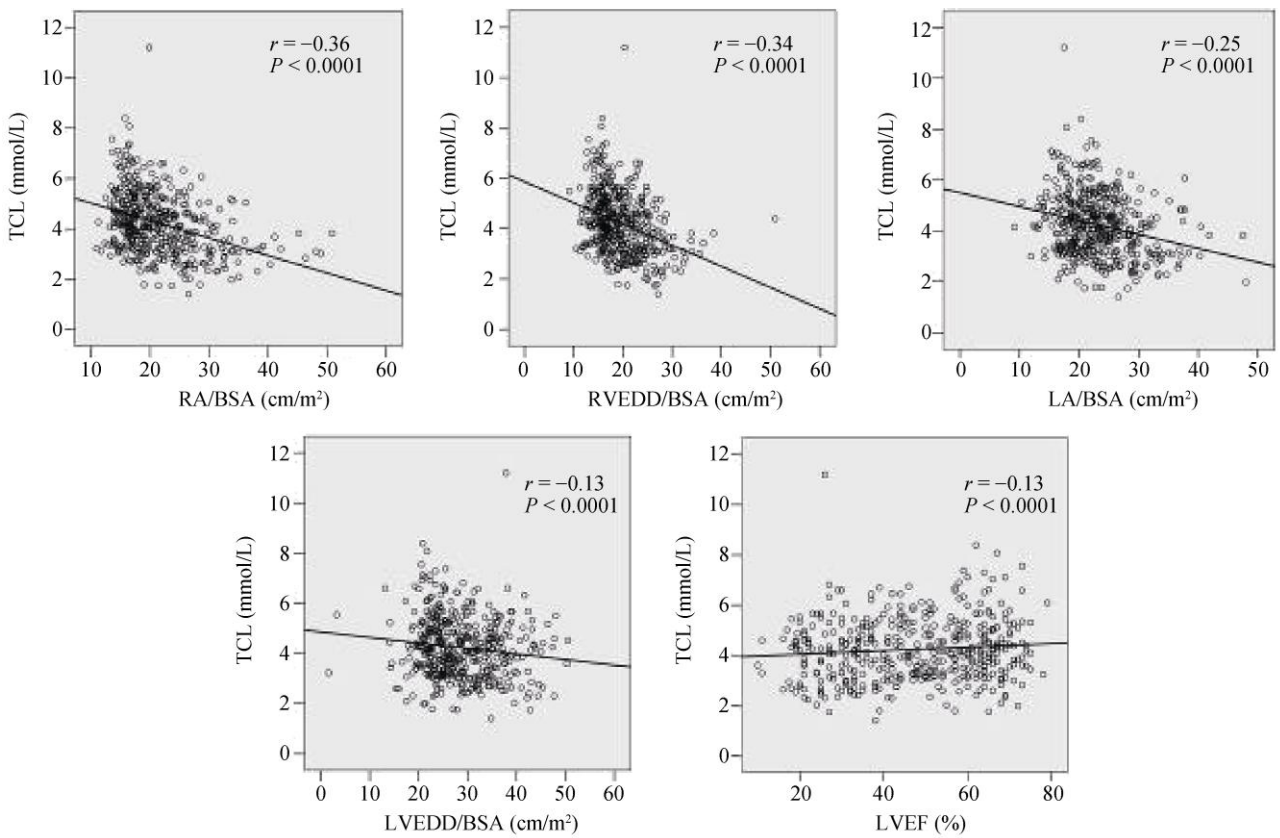

Figure 1. Correlations between total cholesterol and heart chamber size. TCL: total cholesterol; RA: right atrium; BSA: body surface area; RVEDD: right ventricle end diastolic diameter; LA: left atrium; LVEDD: left ventricle end diastolic diameter; LVEF: left ventricular ejection fraction.

Table 2. Correlation between heart chambers and lipid profile in patients with CHF.

	TG	LDL-C	HDL-C	RA/BSA	RVEDD/BSA	LA/BSA	LVEDD/BSA	LVEF
TCL	0.351#	0.896#	0.305#	–0.361#	–0.342#	–0.253#	–0.128#	0.092
TG		0.126#	–0.021	–0.329#	–0.341#	–0.233#	–0.129#	0.020
LDL-C			0.057	–0.247#	–0.211#	–0.155#	–0.090	0.053
HDL-C				–0.135#	–0.148#	–0.092	–0.057	0.102*
RA/BSA					0.804#	0.592#	0.102*	–0.079
RVEDD/BSA						0.546#	0.178#	–0.124#
LA/BSA							0.246#	–0.167#
LVEDD/BSA								–0.644#

*$P < 0.05$; #$P<0.01$, $n = 442$. BSA: body surface area; HDL-C: high-density lipoprotein cholesterol; LA: left atrium; LDL-C: low-density lipoprotein cholesterol; LVEDD: left ventricle end diastolic diameter; LVEF: left ventricular ejection fraction; RA: right atrium; RVEDD: right ventricle end diastolic diameter; TCL: total cholesterol; TG: triglyceride.

Table 3. Correlations between heart chamber size and lipid profile in CHF patients with preserved LVEF.

	TG	LDL-C	HDL-C	RA/BSA	RVEDD/BSA	LA/BSA	LVEDD/BSA
TCL	0.305#	0.893#	0.363#	–0.332#	–0.287#	–0.283#	–0.084
TG		0.090	–0.089	–0.311#	–0.316#	–0.186#	–0.185#
LDL-C			0.099	–0.203#	–0.141*	–0.214#	–0.027
HDL-C				–0.164*	–0.187#	–0.083	–0.053
RA/BSA					0.847#	0.569#	0.177*
RVEDD/BSA						0.517#	0.222#
LA/BSA							0.255#

*$P < 0.05$; #$P < 0.01$; $n = 245$. BSA: body surface area; CHF: congestive heart failure; HDL-C: high-density lipoprotein cholesterol; LA: left atrium; LDL-C: low-density lipoprotein cholesterol; LVEDD: left ventricle end diastolic diameter; LVEF: left ventricular ejection fraction; RA: right atrium; RVEDD: right ventricle end diastolic diameter; TCL: total cholesterol; TG: triglyceride.

Table 4. Correlations between heart chamber size and lipid profile in CHF patients with systolic dysfunction.

	TG	LDL-C	HDL-C	RA/BSA	RVEDD/BSA	LA/BSA	LVEDD/BSA
TCL	0.418#	0.899#	0.272#	–0.382#	–0.379#	–0.227#	–0.147*
TG		0.172#	0.035	–0.371#	–0.388#	–0.303#	–0.094
LDL-C			0.029	–0.276#	–0.259#	–0.112	–0.142*
HDL-C				–0.118	–0.121	–0.086	–0.016
RA/BSA					0.779#	0.606#	0.023
RVEDD/BSA						0.558#	0.094
LA/BSA							0.159*

*$P < 0.05$; #$P < 0.01$; $n = 197$. BSA: body surface area; CHF: congestive heart failure; HDL-C: high-density lipoprotein cholesterol; LA: left atrium; LDL-C: low-density lipoprotein cholesterol; LVEDD: left ventricle end diastolic diameter; LVEF: left ventricular ejection fraction; RA: right atrium; RVEDD: right ventricle end diastolic diameter; TCL: total cholesterol; TG: triglyceride.

3.2 Patients with preserved systolic function versus patients with systolic dysfunction

In the subgroup analysis, the results were consistent with the previous findings that the strongest correlation for lipid levels was with RVEDD and RA, irrespective of the left ventricle systemic function (Tables 3 & 4). However, the correlation between lipid levels and LA were weaker in both subgroups. In patients with preserved LVEF as well as those with LV systolic dysfunction, there was no correlation between LVEDD and lipid levels such as TCL, LDL-C, and HDL-C.

3.3 Patients receiving statin therapy *vs.* patients not receiving statin therapy

The correlation between lipid profile and RVEDD and size of RA were similar in patients with CHF with or without statin treatment (Tables 5 & 6). However, the correlation between lipid levels and size of LA was weaker in both subgroups. In addition, there was no cor-

relation between LVEDD and lipid levels such as TCL, LDL-C, and HDL-C in patients with CHF irrespective of whether or not they were receiving statin therapy.

3.4 Partial correlation and linear regression between lipid profile and echocardiographic parameters

The correlation between lipid profile and size of the right heart remained unchanged in partial correlation in which age, gender, smoking status, New York Heart Association (NYHA) functional class, comorbidities and medication use were taken as co-variables (Table 7). In multiple linear regression models, standardized coefficients were calculated. Finally, the relationship between lipid levels and echocardiographic parameters was established, which was consistent with unadjusted results (Table 8).

Table 5. Correlations between heart chamber size and lipid profile in CHF patients not receiving statin therapy.

	TG	LDL-C	HDL-C	RA/BSA	RVEDD/BSA	LA/BSA	LVEDD/BSA
TCL	0.339#	0.886#	0.278#	–0.330#	–0.283#	–0.255#	–0.108
TG		0.067	–0.026	–0.340#	–0.351#	–0.308#	–0.136*
LDL-C			0.029	–0.204#	–0.145*	–0.135*	–0.069
HDL-C				–0.119*	–0.118*	–0.086	–0.052
RA/BSA					0.774#	0.608#	0.152*
RVEDD/BSA						0.545#	0.177#
LA/BSA							0.226#

*$P < 0.05$; #$P < 0.01$; $n = 284$. BSA: body surface area; CHF: congestive heart failure; HDL-C: high-density lipoprotein cholesterol; LA: left atrium; LDL-C: low-density lipoprotein cholesterol; LVEDD: left ventricle end diastolic diameter; LVEF: left ventricular ejection fraction; RA: right atrium; RVEDD: right ventricle end diastolic diameter; TCL: total cholesterol; TG: triglyceride.

Table 6. Correlations between heart chamber size and lipid profile in patients receiving statin therapy.

	TG	LDL-C	HDL-C	RA/BSA	RVEDD/BSA	LA/BSA	LVEDD/BSA
TCL	0.370#	0.922#	0.387#	–0.403#	–0.456#	–0.233#	–0.178*
TG		0.222#	–0.020	–0.310#	–0.330#	–0.121	–0.126
LDL-C			0.137	–0.321#	–0.356#	–0.187*	–0.143
HDL-C				–0.178*	–0.237#	–0.099	–0.082
RA/BSA					0.867#	0.560#	0.030
RVEDD/BSA						0.545#	0.184*
LA/BSA							0.295#

*$P < 0.05$; #$P < 0.01$; $n = 158$. BSA: body surface area; HDL-C: high-density lipoprotein cholesterol; LA: left atrium; LDL-C: low-density lipoprotein cholesterol; LVEDD: left ventricle end diastolic diameter; LVEF: left ventricular ejection fraction; RA: right atrium; RVEDD: right ventricle end diastolic diameter; TCL: total cholesterol; TG: triglyceride.

Table 7. Partial correlations between heart chamber size and lipid profile in patients with CHF.

	TG	LDL-C	HDL-C	RA/BSA	RVEDD/BSA	LA/BSA	LVEDD/BSA
TCL	0.350#	0.871 #	0.356#	–0.283#	–0.379#	–0.082	–0.045
TG		0.109	–0.117	–0.2880#	–0.276#	–0.078	–0.065
LDL-C			0.006	–0.237*	–0.301#	–0.087	–0.131
HDL-C				0.033	0.033	0.051	–0.105
RA/BSA					0.806#	0.021*	–0.056
RVEDD/BSA						0.267#	0.034
LA/BSA							0.346#

*$P < 0.05$; #$P < 0.01$; $n = 442$. BSA: body surface area; HDL-C: high-density lipoprotein cholesterol; LA: left atrium; LDL-C: low-density lipoprotein cholesterol; LVEDD: left ventricle end diastolic diameter; LVEF: left ventricular ejection fraction; RA: right atrium; RVEDD: right ventricle end diastolic diameter; TCL: total cholesterol; TG: triglyceride.

Table 8. Linear regression of lipid profile and echocardiographic parameters.

Dependent variables	Predictor	Standardized coefficient	*P* value
TCL	RA/BSA	-0.361	< 0.001
TG	RV/BSA	-0.357	< 0.001
HDL-C	RV/BSA	-0.145	< 0.001
LDL-C	RA/BSA	-0.247	< 0.001

TCL: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.

4 Discussion

Our study showed that there was an inverse relationship between lipid levels and RA or RVEDD, which was independent of LVEF and heart failure type. This relationship did not exist in patients with coronary heart disease without CHF or with neither CAD nor CHF (unpublished data). This relationship suggested that volume overload might play an important role in lipid metabolism in CHF. To the best of our knowledge, this is the first study providing these results or similar data under a similar setting. We used the following Medical Subject Heading (MeSH) terms: cholesterol, or (cholesterol, LDL), or (cholesterol, HDL), or triglycerides with heart failure to perform a literature search. The search was limited to human studies and clinical trials. Findings similar to this study were not found.

Elevated serum cholesterol levels were shown to be a risk factor for the development of CHF in the Framingham study.[5] However, subsequent clinical observational studies suggest that low lipid levels are associated with worse clinical outcomes in CHF, and the inverse relationship between lipid levels and adverse clinical outcomes has been consistently documented in clinical studies.[11–13,17] Three major randomized trials, COntrolled ROsuvastatin multi-NAtional trial in heart failure (CORONA), Gruppo Italiano per lo Studio della Sopravvivenza nell'Insufficienza Cardiaca (GISSI-HF) and the pitavastatin heart failure study (PEARL study) have directly addressed the issue about lipid lowering therapy in patients with CHF, and failed to show any beneficial clinical effect on mortality in such patients.[8–10] Despite the neutral effect on all-cause or cardiovascular mortality, the efficacy and safety of statin therapy in patients with CHF is still a matter of debate.[18,19] Evidence has shown that statin therapy significantly decreases the rate of hospitalization for worsening CHF and increases LVEF compared with placebo.[8,19] Our understanding of lipid metabolism in heart failure is certainly incomplete. Several possible mechanisms have been proposed.

Decreased calorie intake and food absorption might be possible reasons for low lipid levels in CHF. In addition, CHF is a metabolically demanding condition. The resting metabolic rate accounts for up to 70% of daily energy expenditure in CHF.[20] Increased cardiac and breathing work in chronic heart failure leads to a greater resting metabolic rate and the presence of a catabolic state. In addition, there are several reasons for a worsened nutrition status in patients with CHF.[21] First, salt restrictions may result in loss of appetite as food loses its appeal and taste, and fluid restrictions may cause an increase in thirst. Second, patients with CHF also have symptoms that can affect their food intake, for example gastrointestinal symptoms like nausea, loss of appetite, or an early feeling of satisfaction. Third, drugs such as digoxin usually affect food intake and minor degrees of digitalis intoxication can cause anorexia, nausea, and diarrhea.

In addition to the above factors causing malnutrition, venous congestion in the stomach and intestines may play a role in lipid metabolism. It not only leads to hypomotility in the gastrointestinal tract, but also reduces nutrition and bile acid absorption. In order to balance the loss of bile acids, cholesterol is converted by the liver into bile acids, further lowering the level of cholesterol in the body.[3] The right ventricular (RV) is highly sensitive to the volume status, thus, it is a good indicator for chronic volume load status.[22]

The RV is a thin-walled structure. Unlike left ventricular (LV), RV is able to accommodate varying degree of preload (volume load) without affecting its cardiac output because RV can distend its free wall without evoking the Frank-Starling mechanism to augment cardiac output.[23] The RV only relies on the Frank-Starling mechanism to augment cardiac output when a large increase in volume occurs, therefore, RV dilation is more sensitive to volume overload. The RA, being a thin-walled chamber, is also very sensitive to chronic volume overload. In addition, tricuspid regurgitation (TR) also contributes to venous congestion in heart failure. Our finding that CHF patients with severe TR had much lower lipid level than those patients without TR (unpublished data) supports the above notion. The obvious inverse relationship between lipid levels and size of RA, or RV presented in the study, indicates the importance of volume overload, i.e., venous congestion, in lipid metabolism in CHF. However, the relationship between right chamber diameters and volume status merits further investigation.

Low lipid levels and the larger size of RA and RV in heart failure, however, may simply reflect a greater disease severity. Thus, low lipid levels may just reflect nutritional status that also has a prognostic impact.[24] As for the right heart, investigations have consistently shown

a strong correlation between RV function and mortality in CHF,[25–28] in both ischemic and non-ischemic cardiomyopathy.[26,29] Therefore, either low lipid levels or a larger size of RA or RV may be just markers of disease severity and their relationship may not be causal. Another highly plausible explanation is that patients with low lipid levels may have received more aggressive lipid-lowering treatments in order to achieve overall benefits on cardiac function. However, in the subgroup analysis that included CHF patients either receiving statin therapy or not receiving statin therapy, the observed associations remained unchanged in both the CHF groups. The partial correlation analysis also showed the observed associations remain almost the same when statin therapy was used as the co-variable (unpublished data).

These findings suggest that right heart dysfunction or overload may contribute to the impairment of lipid metabolism. More aggressive therapy aiming at relieving right heart dysfunction or overload may be required for patients with lower lipid profiles. However, the hypothesis warrants further investigation.

There are several limitations to the study. First, this is a cross-sectional study, and our results were generated from a hypothesis that offered potential explanations that lipid-lowering therapy failed to show benefit in patients with CHF. Second, a diminished calorie intake might be another reason for low lipid levels in CHF, but we did not record the weight change or calorie intake. Therefore, our study cannot establish the notion that volume overload is the cause of low cholesterol levels in CHF. More data on venous congestion should have been collected, e.g., diameter of hepatic veins and clinical signs of right heart failure. Third, according to heart failure guidelines, there appears to be an under-treatment with beta-blockers and a frequent treatment with digitalis, which may not reflect the clinical practice in the real world. In the future, it may be possible to analyze the interplay between changes in lipid levels, underlying treatment, and changes in volume status in larger cohorts of patients with standardized follow-up.

Our findings suggest an inverse relationship between lipid levels and RVEDD in CHF; however, because this was an observational study, further investigation is needed to verify our results as well as identify a causal relationship, if any.

Acknowledgements

The work is supported by Hebei Province Government (Hebei Provincial Major Medical Project: LS201315).

References

1 McKelvie RS, Moe GW, Ezekowitz JA, *et al.* The 2012 Canadian Cardiovascular Society heart failure management guidelines update: focus on acute and chronic heart failure. *Can J Cardiol* 2013; 29: 168–181.
2 Giamouzis G, Butler J. Relationship between heart failure and lipids: the paradigm continues to evolve. *J Card Fail* 2007; 13: 254–258.
3 Velavan P, Huan Loh P, Clark A, *et al.* The cholesterol paradox in heart failure. *Congest Heart Fail* Nov-Dec 2007; 13: 336–341.
4 Baigent C, Keech A, Kearney PM, *et al.* Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet* 2005; 366: 1267–1278.
5 Kannel WB, Belanger AJ. Epidemiology of heart failure. *Am Heart J* 1991; 121: 951–957.
6 Velagaleti RS, Massaro J, Vasan RS, *et al.* Relations of lipid concentrations to heart failure incidence: the Framingham Heart Study. *Circulation* 2009; 120: 2345–2351.
7 Ebong IA, Goff DC Jr., Rodriguez CJ, *et al.*Association of lipids with incident heart failure among adults with and without diabetes mellitus: Multiethnic Study of Atherosclerosis. *Circ Heart Fail* 2013; 6: 371–378.
8 Kjekshus J, Apetrei E, Barrios V, *et al*. Rosuvastatin in older patients with systolic heart failure. *N Engl J Med* 2007; 357: 2248–2261.
9 Gissi HFI, Tavazzi L, Maggioni AP, *et al*. Effect of rosuvastatin in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial. *Lancet* 2008; 372: 1231–1239.
10 Takano H, Mizuma H, Kuwabara Y, *et al*. Effects of pitavastatin in Japanese patients with chronic heart failure: the Pitavastatin Heart Failure Study (PEARL Study). *Circ J* 2013; 77: 917–925.
11 Iwaoka M, Obata JE, Abe M, *et al*. Association of low serum levels of apolipoprotein A-I with adverse outcomes in patients with nonischemic heart failure. *J Card Fail* 2007; 13: 247–253.
12 Rauchhaus M, Clark AL, Doehner W, *et al*. The relationship between cholesterol and survival in patients with chronic heart failure. *J Am Coll Cardiol* 2003; 42: 1933–1940.
13 Vredevoe DL, Woo MA, Doering LV, *et al*. Skin test anergy in advanced heart failure secondary to either ischemic or idiopathic dilated cardiomyopathy. *Am J Cardiol* 1998; 82: 323–328.
14 Joles JA, Bongartz LG, Gaillard CA, *et al*. Renal venous congestion and renal function in congestive heart failure. *J Am Coll Cardiol* 2009; 54: 1632.
15 Tian Y, Chen Y, Deng B, *et al*. Serum uric acid as an index of impaired renal function in congestive heart failure. Journal of geriatric cardiology. *J Geriatr Cardiol* 2012; 9: 137–142.

16 Lang RM, Bierig M, Devereux RB, *et al*. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005; 18: 1440–1463.
17 Christ M, Klima T, Grimm W, *et al*. Prognostic significance of serum cholesterol levels in patients with idiopathic dilated cardiomyopathy. *Eur Heart J* 2006; 27: 691–699.
18 De Gennaro L, Brunetti ND, Correale M, *et al*. Statin therapy in heart failure: for good, for bad, or indifferent? *Curr Atheroscler Rep* 2014; 16: 377.
19 Silva S, Lourenco P, Paulo C, *et al*. Statin-induced low cholesterol is not associated with poor outcome in chronic heart failure. *J Cardiovasc Pharmacol Ther* 2012; 17: 284–290.
20 Berry C, Clark AL. Catabolism in chronic heart failure. *Eur Heart J* 2000; 21: 521–532.
21 Jacobsson A, Pihl-Lindgren E, Fridlund B. Malnutrition in patients suffering from chronic heart failure; the nurse's care. *Eur J Heart Fail* 2001; 3: 449–456.
22 Haddad F, Hunt SA, Rosenthal DN, *et al*. Right ventricular function in cardiovascular disease, part I: Anatomy, physiology, aging, and functional assessment of the right ventricle. *Circulation* 2008; 117: 1436–1448.
23 Sayer GT, Semigran MJ. Right ventricular performance in chronic congestive heart failure. *Cardiol Clin* 2012; 30: 271–282.
24 Gastelurrutia P, Lupon J, Domingo M, *et al*. Usefulness of body mass index to characterize nutritional status in patients with heart failure. *Am J Cardiol* 2011; 108: 1166–1170.
25 Testani JM, Khera AV, St John Sutton MG, *et al*. Effect of right ventricular function and venous congestion on cardiorenal interactions during the treatment of decompensated heart failure. *Am J Cardiol* 2010; 105: 511–516.
26 Juilliere Y, Barbier G, Feldmann L, *et al*. Additional predictive value of both left and right ventricular ejection fractions on long-term survival in idiopathic dilated cardiomyopathy. *Eur Heart J* 1997; 18: 276–280.
27 de Groote P, Millaire A, Foucher-Hossein C, et al. Right ventricular ejection fraction is an independent predictor of survival in patients with moderate heart failure. *J Am Coll Cardiol* 1998; 32: 948–954.
28 Di Salvo TG, Mathier M, Semigran MJ, *et al*. Preserved right ventricular ejection fraction predicts exercise capacity and survival in advanced heart failure. *J Am Coll Cardiol* 1995; 25: 1143–1153.
29 Polak JF, Holman BL, Wynne J, *et al*. Right ventricular ejection fraction: an indicator of increased mortality in patients with congestive heart failure associated with coronary artery disease. *J Am Coll Cardiol* 1983; 2: 217–224.