Diabetes, Metabolic Syndrome and Obesity

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ORIGINAL RESEARCH

Association Between Plasma Levels of ANGPTL3, 4, 8 and the Most Common Additional Cardiovascular Risk Factors in Patients with Hypertension

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Background: ANGPTL3, 4 and 8 have been reported to be involved in the regulation of lipid and glucose metabolism. The aim of this study was to investigate the expression of ANGPTL3, 4, 8 in hypertensive patients with or without overweight/obesity, T2D, and hyperlipidemia, and the possible association between their expression and the status of the aforementioned comorbidities.

Methods: Plasma levels of ANGPTL3, 4, and 8 in 87 hospitalized patients with hypertension were measured using ELISA kits. Associations between circulating ANGPTLs levels and the most common additional cardiovascular risk factors were assessed using multivariate linear regression analyses. Pearson's correlation analysis was used to examine the association between ANGPTLs and clinical parameters.

Results: In the context of hypertension, (1) although not statistically significant, circulating ANGPTL3 levels were higher in the overweight/obese group than in the normal weight group; (2) circulating levels of ANGPTL3 and ANGPTL8 were significantly lower in patients with T2D than in non-diabetic patients; (3) circulating ANGPTL3 levels were significantly higher in the hyperlipidemic group than in the non-hyperlipidemic group. ANGPTL3 was associated with T2D and hyperlipidemia status, whereas ANGPTL8 was independently associated with T2D status. In addition, circulating ANGPTL3 levels were positively correlated with TC, TG, LDL-C, HCY, and ANGPTL8, and circulating ANGPTL4 levels were positively correlated with UACR and BNP.

Conclusion: Changes in circulating ANGPTL3 and ANGPTL8 levels have been observed in hypertensive patients with the most common additional cardiovascular risk factors, suggesting a role in the common comorbidities of hypertension and cardiovascular disease. Hypertensive patients with overweight/obesity or hyperlipidemia may benefit from therapies targeting ANGPTL3.

Keywords: angiopoietin-like proteins, hypertension, cardiovascular risk factors, overweight/obesity, type 2 diabetes, hyperlipidemia

Introduction

Hypertension is a major risk factor for cardiovascular disease (CVD).[1] More than 50% of patients with hypertension have additional cardiovascular risk factors, the most common of which are overweight/obesity (40%), diabetes (15%-20%), and lipid disorders (30%).[2] Therefore, they may benefit from molecules that regulate glucose and/or lipid metabolism.

Angiopoietin-like (ANGPTL) proteins are a family of eight secreted proteins with multibiological functions, including regulation of glucose and lipid metabolism.[3,4] ANGPTL3, 4, and 8 are well-characterized endogenous inhibitors of

Received: 20 March 2023
Accepted: 1 June 2023
Published: 7 June 2023

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lipoprotein lipase (LPL) and thus play important roles in lipid homeostasis.[5–9] Many studies have also shown that ANGPTL3, 4 and 8 are increased in obesity and type 2 diabetes (T2D).[10–17] In addition, fewer studies have examined the role of ANGPTL3, 4, and 8 in patients with hypertension. Serum ANGPTL3 is associated with blood pressure,[18] and ANGPTL4 and 8 in both plasma and adipose tissues are increased in hypertensive patients.[19] Several reports have shown that ANGPTL3,[20–22] 4,[23] and 8,[24] are associated with cardiovascular events and thus are emerging cardiovascular biomarkers.[25] Monoclonal antibodies and antisense oligonucleotides targeting ANGPTL3, 4, 8 may therefore be an effective therapeutic strategy for cardiovascular risk reduction.[26]

However, little is known about their expression in and associations with the most common comorbidities of hypertension, ie, obesity, T2D and hyperlipidemia. In the present study, we aim to address these issues, which may shed light on the role of ANGPTL3, 4, and 8 in these patients.

Materials and Methods

Patients

This study included 87 hospitalized hypertensive patients randomly selected in the hypertension department of Henan Provincial People's Hospital from January to December 2020. The study protocol was approved by the Ethics Committee of Henan Provincial People's Hospital (No. 201758) and was conducted in accordance with the Declaration of Helsinki. All patients provided written informed consent to participate in the study.

According to the 2018 Chinese Guidelines for Prevention and Treatment of Hypertension and the 2020 International Society of Hypertension global hypertension practice guidelines,[2] hypertension is defined as an individual's systolic blood pressure (SBP) is ≥ 140 mmHg and/or diastolic blood pressure (DBP) is ≥ 90 mmHg after repeated examination in the office or clinic for all adults (>18 years old). Demographic information, medical history, admission diagnosis, and laboratory data were collected from the electronic medical record system of the hospital. Body mass index (BMI) was calculated as weight (kg) divided by height (m^2). According to the World Health Organization (WHO) guidelines, overweight is defined as BMI 25–29 kg/m^2 and obesity as BMI ≥ 30 kg/m^2.[2,27,28] Based on the Guidelines for the Prevention and Control of Type 2 Diabetes in China (2017 edition), diabetes is defined as fasting plasma glucose ≥ 7.0 mmol/L and/or hemoglobinA1c (HbA1c) ≥ 6.5%. Hyperlipidemia is defined according to the Guidelines for Prevention and Treatment of Dyslipidemia in Chinese Adults (revised in 2016). Patients with type 1 diabetes; psychiatric, behavioral, or cognitive disorders; stroke; heart failure; significant pre-existing organ dysfunction; use of medications or supplements known to affect body composition or bone mass; use of special diets or nutritional interventions; participation in any vigorous exercise or professional sports within the previous six months; and pregnant women were excluded from the study.

Blood Collection

After a 12-hour overnight fast, whole blood was collected in ethylenediaminetetraacetic acid tubes and centrifuged at 3000 rpm for 5 minutes at room temperature. Plasma samples were then stored at −80°C until use.

Determination of Plasma ANGPTLs Concentrations

Plasma ANGPTL concentrations were determined by enzyme-linked immunosorbent assay (ELISA). ELISA kits for ANGPTL3 (Catalog No. 1699h), ANGPTL4 (Catalog No. 2085h), ANGPTL8 (Catalog No. 11644h) were purchased from EIAab, Wuhan, China, with sensitivities of 0.1 ng/mL, 0.044 ng/mL, and 32 pg/mL, respectively. The intra- and inter-assay coefficients of variation (CV%) values were ≤ 5.9% and ≤ 9.8% for the ANGPTL3 kit, ≤ 5.6% and ≤ 7.7% for the ANGPTL4 kit, and ≤ 6.5% and ≤ 9.2% for the ANGPTL8 kit, respectively.

Statistical Analysis

All data were analyzed using SPSS version 22.0 software (IBM Corp., Armonk, NY). Normally distributed data were expressed as the mean ± standard deviation (SD), unless otherwise noted, and comparisons between patient groups were made using the Student's independent *t*-test (two-tailed). Multivariate linear regression analysis was performed to examine the associations between circulating ANGPTLs levels and disease status. Pearson's correlation analysis was used to examine the correlation between ANGPTLs and clinical parameters. $P < 0.05$ was considered statistically significant.

Results

Increased ANGPTL3 in Overweight/Obese Compared to Non-Overweight/Obese Hypertensive Patients

In this study, 32 out of 87 (36.8%) hypertensive patients had an overweight/obese BMI. As shown in Table 1, hypertensive patients with overweight/obesity had significantly higher BMI (29.04 ± 3.52 kg/m^2 vs 22.36 ± 2.17 kg/m^2, $P < 0.001$) but lower HDL-C levels (1.04 ± 0.20 mmol/L vs 1.25 ± 0.31 mmol/L, $P = 0.004$) compared with those without overweight/obesity. In addition, although circulating ANGPTL3 concentrations were higher in overweight/obese subjects (168.40 ± 19.72 ng/mL vs 119.57 ± 20.11 ng/mL, $P = 0.09$), this was not statistically significant (Table 1, Figure 1).

Decreased ANGPTL3 and ANGPTL8 in Diabetic Compared to Non-Diabetic Hypertensive Patients

In the present study, 19 out of 87 (21.8%) hypertensive patients had T2D. The characteristics of the diabetic and non-diabetic hypertensive patients are shown in Table 2. Type 2 diabetic hypertensive patients were older (60.47 ± 8.22 years vs 47.55 ± 16.11 years, $P = 0.001$) and had higher FBG (7.27 ± 3.54 mmol/L vs 4.77 ± 1.17 mmol/L, $P < 0.001$) and HbA1c [(7.92 ± 1.65)% vs (5.96 ± 0.91)%, $P < 0.001$] but lower DBP (83.63 ± 17.53 pg/mL vs 94.92 ± 20.79 mmHg, $P = 0.03$) than non-diabetic hypertensive patients (Table 2).

Surprisingly, circulating levels of ANGPTL3 and ANGPTL8 were significantly lower in patients with T2D than in non-diabetic hypertensive patients (61.51 ± 9.55 ng/mL vs 159.94 ± 14.46 ng/mL, $P < 0.001$; 254.57 ± 19.66 pg/mL vs 389.75 ± 31.71 pg/mL, $P = 0.03$), whereas there was no significant difference in ANGPTL4 levels between the two groups (5.80 ± 0.41 ng/mL vs 5.60 ± 0.40 ng/mL, $P = 0.80$; Table 2, Figure 2).

Table 1 Characteristics of Hypertensive Patients According to Overweight/Obese Status

Variables	Non-Overweight/Obesity Hypertension (N = 24)	Overweight/Obesity Hypertension (N = 32)	*P* value
Age (years)	50.83 ± 17.28	49.44 ± 14.95	0.75
BMI (kg/m^2)	22.36 ± 2.17	29.04 ± 3.52	< 0.001***
SBP (mmHg)	151.67 ± 26.45	156.00 ± 28.49	0.56
DBP (mmHg)	89.79 ± 23.06	92.91 ± 20.11	0.59
HR (beats/min)	87.75 ± 16.02	82.19 ± 15.22	0.19
TC (mmol/L)	4.68 ± 0.99	4.57 ± 1.08	0.69
TG (mmol/L)	1.70 ± 1.28	1.98 ± 1.14	0.40
HDL-C (mmol/L)	1.25 ± 0.31	1.04 ± 0.20	0.004**
LDL-C (mmol/L)	2.79 ± 0.84	2.76 ± 0.90	0.90
FBG (mmol/L)	5.38 ± 1.72	5.35 ± 1.97	0.94
HbA1C (%)	6.48 ± 1.66	6.57 ± 1.50	0.85
ANGPTL3 (ng/mL)	119.57 ± 20.11	168.40 ± 19.72	0.09
ANGPTL4 (ng/mL)	5.25 ± 1.12	5.54 ± 1.43	0.42
ANGPTL8 (pg/mL)	362.59 ± 41.53	390.01 ± 48.15	0.68

Notes: The results of circulating ANGPTLs levels were expressed as mean ± standard error of the mean (SEM). Other data were expressed as mean ± SD. Differences between groups were evaluated by independent *t*-test. **$P < 0.01$; ***$P < 0.001$.
Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; TC, total cholesterol, TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FBG, fasting blood glucose; HbA1c, hemoglobin A1c; ANGTPL3, angiopoietin-like protein 3; ANGTPL4, angiopoietin-like protein 4; ANGTPL8, angiopoietin-like protein 8.

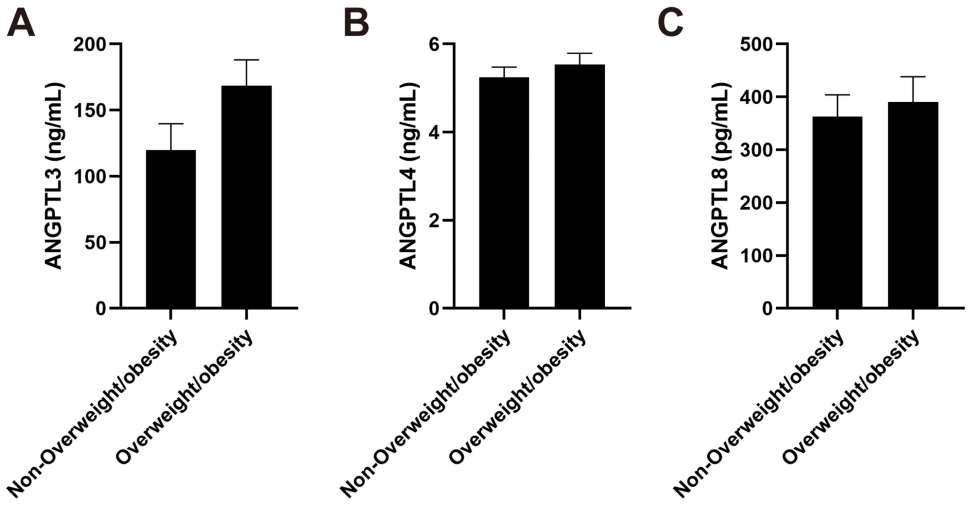

Figure 1 Circulating levels of (A) ANGPTL3, (B) ANGPTL4, and (C) ANGPTL8 in hypertensive patients with or without overweight/obesity.

Increased ANGPTL3 in Hyperlipidemic Compared to Non-Hyperlipidemic Hypertensive Patients

In this study, 37 out of 87 (42.5%) hypertensive patients had hyperlipidemia. The characteristics of the hyperlipidemic and non-hyperlipidemic hypertensive patients are shown in Table 3. Hyperlipidemic hypertensive patients had higher BMI (27.62 ± 4.35 kg/m^2 vs 24.87 ± 4.35 kg/m^2, $P = 0.02$), TC (4.89 ± 0.94 mmol/L vs 4.17 ± 1.01 mmol/L, $P = 0.001$), TG (2.50 ± 1.26 mmol/L vs 1.31 ± 0.67 mmol/L, $P < 0.001$), LDL-C (3.02 ± 0.83 mmol/L vs 2.46 ± 0.79 mmol/L, $P = 0.002$) and DBP (98.38 ± 20.08 mmHg vs 88.45 ± 19.60 mmHg, $P = 0.03$) but lower HDL-C (1.01 ± 0.15 mmol/L vs 1.17 ± 0.30 mmol/L, $P = 0.002$) levels than non-hyperlipidemic hypertensive patients.

Table 2 Characteristics of Hypertensive Patients According to Diabetes Status

Variables	Non-Diabetics Hypertension (N = 66)	T2D Hypertension (N = 19)	*P* value
Age (years)	47.55 ± 16.11	60.47 ± 8.22	< 0.001***
BMI (kg/m^2)	26.22 ± 4.83	26.00 ± 3.06	0.88
SBP (mmHg)	155.20 ± 27.07	151.68 ± 23.69	0.61
DBP (mmHg)	94.92 ± 20.79	83.63 ± 17.53	0.03*
HR (beats/min)	83.21 ± 15.14	77.21 ± 10.32	0.11
TC (mmol/L)	4.53 ± 1.03	4.46 ± 1.14	0.79
TG (mmol/L)	1.87 ± 1.11	1.74 ± 1.27	0.67
HDL-C (mmol/L)	1.09 ± 0.25	1.13 ± 0.29	0.61
LDL-C (mmol/L)	2.77 ± 0.84	2.60 ± 0.93	0.46
FBG (mmol/L)	4.77 ± 1.17	7.27 ± 3.54	0.007**
HbA1C (%)	5.96 ± 0.91	7.92 ± 1.65	0.001**
ANGPTL3 (ng/mL)	159.94 ± 14.46	61.51 ± 9.55	< 0.001***
ANGPTL4 (ng/mL)	5.60 ± 0.40	5.80 ± 0.41	0.80
ANGPTL8 (pg/mL)	389.75 ± 31.71	254.57 ± 19.66	0.001**

Notes: The results of circulating ANGPTLs levels were expressed as mean ± SEM. Other data were expressed as mean ± SD. Differences between groups were evaluated by independent *t*-test. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; TC, total cholesterol, TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FBG, fasting blood glucose; HbA1c, hemoglobin A1c; ANGTPL3, angiopoietin-like protein 3; ANGTPL4, angiopoietin-like protein 4; ANGTPL8, angiopoietin-like protein 8.

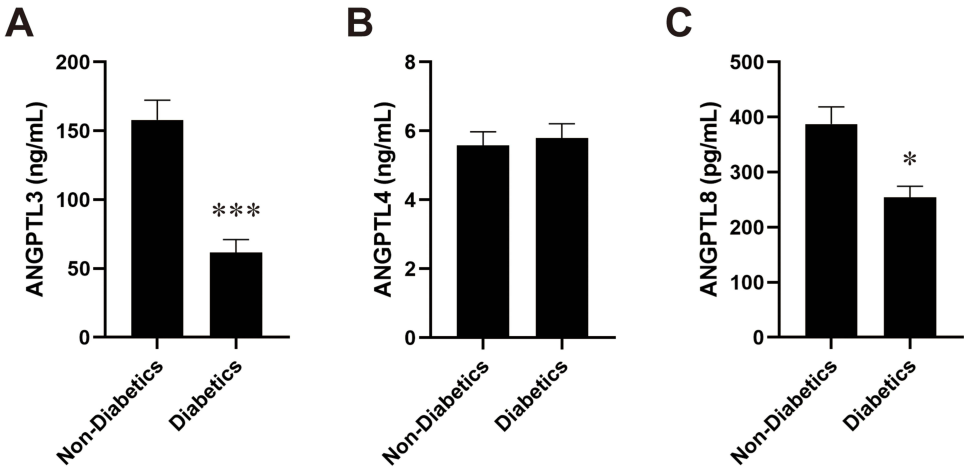

Figure 2 Circulating levels of (**A**) ANGPTL3, (**B**) ANGPTL4, and (**C**) ANGPTL8 in hypertensive patients with or without T2D. *$P < 0.05$; ***$P < 0.001$.

In patients with hyperlipidemia, circulating levels of ANGPTL3 were significantly higher than in hypertensive patients without hyperlipidemia (166.31 ± 17.82 ng/mL vs 116.86 ± 16.58 ng/mL, $P = 0.047$), whereas there were no significant differences in ANGPTL4 and ANGPTL8 levels between the two groups (5.27 ± 0.24 ng/mL vs 5.87 ± 0.54 ng/mL, $P = 0.36$; 354.50 ± 28.91 pg/mL vs 367.20 ± 40.62 pg/mL, $P = 0.81$; Table 3, Figure 3).

Association of Circulating ANGPTL3, 4, and 8 Levels with the Most Common Additional Cardiovascular Risk Factors in Hypertension

The associations between circulating ANGPTL3, 4, and 8 levels and the most common additional cardiovascular risk factors (overweight/obesity, diabetes, hyperlipidemia) in the context of hypertension were examined using

Table 3 Characteristics of Hypertensive Patients According to Hyperlipidemia Status

Variables	Non-Hyperlipidemia Hypertension (N = 47)	Hyperlipidemia Hypertension (N = 37)	*P* value
Age (years)	51.57 ± 17.45	48.57 ± 13.01	0.39
BMI (kg/m^2)	24.87 ± 4.35	27.62 ± 4.35	0.02*
SBP (mmHg)	149.91 ± 22.79	160.89 ± 29.21	0.06
DBP (mmHg)	88.45 ± 19.60	98.38 ± 20.08	0.03*
HR (beats/min)	80.32 ± 12.25	83.86 ± 16.83	0.29
TC (mmol/L)	4.17 ± 1.01	4.89 ± 0.94	0.001**
TG (mmol/L)	1.31 ± 0.67	2.50 ± 1.26	< 0.001***
HDL-C (mmol/L)	1.17 ± 0.30	1.01 ± 0.15	0.002**
LDL-C (mmol/L)	2.46 ± 0.79	3.02 ± 0.83	0.002**
FBG (mmol/L)	4.99 ± 1.51	5.80 ± 2.82	0.10
HbA1C (%)	6.18 ± 1.17	6.58 ± 1.54	0.24
ANGPTL3 (ng/mL)	116.86 ± 16.58	166.31 ± 17.82	0.047*
ANGPTL4 (ng/mL)	5.87 ± 0.54	5.27 ± 0.24	0.36
ANGPTL8 (pg/mL)	367.20 ± 40.62	354.50 ± 28.91	0.81

Notes: The results of circulating ANGPTLs levels were expressed as mean ± SEM. Other data were expressed as mean ± SD. Differences between groups were evaluated by independent *t*-test. *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.
Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; TC, total cholesterol, TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; FBG, fasting blood glucose; HbA1c, hemoglobin A1c; ANGTPL3, angiopoietin-like protein 3; ANGTPL4, angiopoietin-like protein 4; ANGTPL8, angiopoietin-like protein 8.

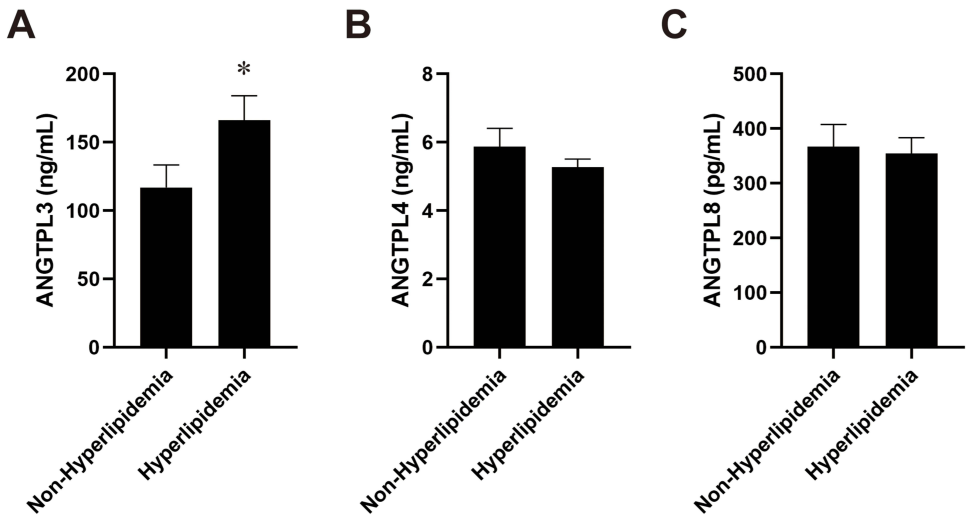

Figure 3 Circulating levels of (**A**) ANGPTL3, (**B**) ANGPTL4, and (**C**) ANGPTL8 in hypertensive patients with or without hyperlipidemia. *$P < 0.05$.

multiple linear regression and the results are shown in Table 4. Circulating ANGPTL3 levels were significantly associated with diabetes and hyperlipidemia status, whereas ANGPTL8 levels were independently associated with diabetes status. However, ANGPTL4 levels were not associated with these cardiovascular risk factors.

Table 4 Multiple Linear Regression Analysis of ANGPTLs

Variables	Unstandardized Coefficients		Standardized Coefficients	t	*P*
	B	Standard Error	Beta		
Dependent variable: ANGTPL3					
Constant	156.491	98.386		1.591	0.118
Sex	−48.252	27.169	−0.222	−1.776	0.082
Age	0.744	0.901	0.109	0.825	0.413
BMI	0.565	3.030	0.024	0.186	0.853
Diabetes (yes/no)	−132.365	34.356	−0.492	−3.853	< 0.001***
Hyperlipidemia (yes/no)	76.665	27.243	0.356	2.814	0.007**
Dependent variable: ANGTPL4					
Constant	3.908	1.293		3.021	0.004
Sex	−0.041	0.357	−0.017	−0.116	0.908
Age	0.028	0.012	0.353	2.328	0.024*
BMI	0.004	0.040	0.014	0.099	0.922
Diabetes (yes/no)	0.011	0.452	0.003	0.023	0.981
Hyperlipidemia (yes/no)	0.056	0.358	0.023	0.156	0.877
Dependent variable: ANGTPL8					
Constant	291.742	258.847		1.127	0.265
Sex	−42.720	71.480	−0.087	−0.598	0.553
Age	3.004	2.372	0.195	1.266	0.211
BMI	1.228	7.972	0.023	0.154	0.878
Diabetes (yes/no)	−198.195	90.388	−0.327	−2.193	0.033*
Hyperlipidemia (yes/no)	20.046	71.674	0.041	0.280	0.781

Notes: *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.
Abbreviations: BMI, body mass index; ANGTPL3, angiopoietin-like protein 3; ANGTPL4, angiopoietin-like protein 4; ANGTPL8, angiopoietin-like protein 8.

Pearson's Correlation Analysis

Correlations between plasma ANGPTLs concentrations and other biochemical characteristics of hypertensive patients were determined by Pearson's correlation analysis. The results are shown in Supplementary Table S1. In the context of hypertension, a significant negative correlation was found between circulating ANGPTL3 levels and age (r = −0.216, $P = 0.044$), whereas significant positive correlations were found between circulating ANGPTL3 levels and TC (r = 0.233, $P = 0.034$), TG (r = 0.288, $P = 0.008$), LDL-C (r = 0.227, $P = 0.039$), homocysteine (HCY, r = 0.338, $P = 0.007$), and ANGPTL8 (r = 0.589, $P < 0.001$). A significant negative correlation was found between circulating ANGPTL4 levels and calcium (r = - 0.298, $P = 0.006$), whereas significant positive correlations were observed between circulating ANGPTL4 levels and urinary microalbumin to creatinine ratio (UACR, r = 0.477, $P = 0.001$) and brain natriuretic peptide (BNP, r = 0.721, $P = 0.028$), respectively. However, no correlation was found between ANGPTL8 and other biochemical characteristics except for ANGPTL3 in patients with hypertension.

Discussion

ANGPTLs are a family of eight metabolic proteins with multibiological properties including established roles in glucose and lipid metabolism.[3,4] Expression characteristics of ANGPTL3, 4, 8 in metabolic diseases such as obesity, T2D and hyperlipidemia have been well studied. However, fewer studies have investigated the role of ANGPTL3, 4, 8 in hypertension. Serum ANGPTL3 is associated with blood pressure.[18] ANGPTL4 and ANGPTL8 are increased in patients with hypertension.[19]

It is well established that TG concentrations are positively associated with cardiovascular events.[29,30] ANGPTL3, ANGPTL4, and ANGPTL8 are physiological inhibitors of LPL, thereby regulating lipoprotein and triglyceride metabolism.[5,6] Inhibition of ANGPTL3 has been reported to be associated with a reduced risk of cardiovascular disease.[31] In patients with coronary artery disease, ANGPTL4 and ANGPTL8 may predict cardiovascular events.[23,24] ANGPTL3, ANGPTL4, and ANGPTL8 are potential therapeutic targets for hypertriglyceridemia and cardiovascular risk reduction.[26] Hypertension is often accompanied by additional cardiovascular risk factors:[2] obesity,[32,33] T2D,[34,35] and lipid disorders.[2,36,37] In this study, 36.8%, 21.8%, and 42.5% of hypertensive patients have overweight/obesity, T2D and hyperlipidemia, respectively. Therefore, research focusing on ANGPTL3, 4, 8 expression in and associations with the above common comorbidities of hypertension has great significance for these patients.

First, there were no statistically significant differences in plasma ANGPTL3, 4, 8 concentrations between overweight/obese and non-overweight/obese hypertensive patients, although obesity is a major risk factor for hypertension.[2,38] Increased levels of ANGPTL3 were observed, although not statistically significant, which may be due to the small sample size. Previous studies have found that ANGPTL3, 4 and 8 are increased in obesity.[10,17,18,39] These results suggest that hypertensive patients with overweight/obesity may benefit from therapies targeting ANGPTL3.

Second, ANGPTL3 and ANGPTL8 were surprisingly significantly lower in T2D patients than in non-diabetic patients, respectively, whereas circulating ANGPTL4 was not significantly different between the two groups. Previous studies have shown increased circulating levels of ANGPTL3 and ANGPTL4 in subjects with vs without T2D.[10] In addition, several studies have investigated circulating levels of ANGPTL8 in T2D with mixed results. Most studies reported that ANGPTL8 levels were significantly higher in T2D,[16,40–44] while other studies observed decreased,[45,46] or unchanged ANGPTL8 levels.[47,48] Apart from the difference in ELISA kits, elucidating the mechanism of ANGPTLs, especially ANGPTL8, in T2D may help to understand these mixed results.

Third, circulating ANGPTL3 levels were significantly higher in hyperlipidemic patients than in non-hyperlipidemic patients. In addition, circulating ANGPTL3 levels were positively associated with the lipid profile: TC, TG and LDL-C in hypertensive patients. Consistent with this, previous studies have observed positive correlations between them.[18,49] ANGPTL3 is a promising therapeutic target for dyslipidemia.[50–52]

In addition, circulating ANGPTL3 levels were associated with hyperlipidemia status in the context of hypertension. Therefore, emerging therapeutic strategies targeting ANGPTL3 may benefit hypertensive patients with hyperlipidemia and reduce the cardiovascular risk.[26]

However, this study was limited by a small sample size. Replication studies with independent, larger samples are needed to confirm these findings. In addition, the roles of ANGPTL3 and ANGPTL8 may be different and even opposite between T2D and hypertension, which remains unclear.

Conclusion

Changes in circulating ANGPTL3 and ANGPTL8 levels have been observed in hypertensive patients with the most common additional cardiovascular risk factors, suggesting a role in the common comorbidities of hypertension and cardiovascular disease. Hypertensive patients with overweight/obesity or hyperlipidemia may benefit from therapies targeting ANGPTL3.

Funding

This work was funded by the Health Commission of Henan Province (No. LHGJ20190590 and LHGJ20220083) and the Natural Science Foundation of Henan Province (202300410411).

Disclosure

The authors report no conflicts of interest in this work.

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