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Mechanism of action of Profilin-1 and Fibulin-3 in vascular remodeling in hypertensive rats

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Abstract. – OBJECTIVE: This paper aims to investigate the expressions of Fibulin-3 and Profilin-1 in vascular remodeling and the relationship between the two factors and vascular remodeling in hypertensive rats.

MATERIALS AND METHODS: 45 spontaneously hypertensive rats (SHR) and 15 healthy Wistar Kyoto (WKY) rats were collected. The 45 SHR were randomly divided into group A, group B, and group C. Group A was injected with Profilin-1 overexpression of adenoviral vector of pAd-Profilin-1-RES-EGFP; group B was injected with recombinant Fibulin3 protein solution; and group C was injected with normal saline. The rats in the control group were normally raised. All rats were anesthetized and dissected, and the thoracic aorta of rats was taken out at T0 (8 weeks old), T1 (12 weeks old), T2 (16 weeks old). The expressions of Fibulin-3 and Profilin-1 protein in the thoracic aorta were analyzed by Western blot. The overexpression of Profilin-1 and Fibulin-3 protein, blood pressure, and body weight were compared.

RESULTS: The expression level and systolic blood pressure of Profilin-1 protein of rats in group A were significantly higher than those in the other two groups ($p<0.05$). The expression level of Fibulin-3 protein of rats in group B at T2 was significantly higher than that in the other two groups ($p<0.05$). The thickness of vascular wall in the control group and group C at T1 and T2 was significantly lower than that of group A and group B. The vascular wall/cavity ratio of rats in group A, B, C was significantly higher than that in the control group at T1 and T2 ($p<0.001$).

CONCLUSIONS: The changes in Profilin-1 and Fibulin-3 levels may affect the occurrence and development of vascular remodeling in hypertension. Therefore, Profilin-1 and Fibulin-3 can be used as sensitive detection indices for hypertension vascular remodeling.

Key Words:
Profilin-1, Fibulin03, Hypertensive rats, Vascular remodeling.

Introduction

Hypertension is one of the most common cardiovascular diseases[1]. The occurrence and development of hypertension is accompanied by the changes in vascular structure and function, which are classified as the revascularization of hypertension, a major feature of hypertension. It has been found that vascular remodeling plays an important role in the occurrence and development of hypertension, and a vicious circulation is formed by the interaction of hypertension and vascular remodeling[2,3].

The changes in vascular matrix components are the important causes of vascular remodeling[4]. Proline, a class of actin regulatory protein whose profilin-1 is expressed in cardiovascular tissues, is a key actin regulatory protein[5]. Related studies have shown that profilin-1 plays a direct role in vascular remodeling and myocardial injury, and is an important factor in promoting myocardial dysfunction, which is closely related to cardiac hypertrophy[6,7]. It has been confirmed that the interference with the expression of profilin-1 can reduce the degree of myocardial fiber and improve the state of cardiac hypertrophy[8]. Fibulin-3, a member of the Fibulin family of extracellular matrix proteins, has an important effect on maintaining the integrity of the basement membrane and the binding of other extracellular matrices, such as elastic fiber and basement membrane[9]. Therefore, this paper discusses the expression and correlation of Fibulin-3 and Profilin-1 in vascular remodeling in hypertensive rats, and provides a basis for clinical prevention of hypertension vascular remodeling.

Materials and Methods

Laboratory Animals and Specimen Sources

Object: 45 male spontaneously hypertensive rats (SHR) aged 8 weeks old and 15 healthy Wistar Kyoto (WKY) rats of the same age were purchased from Beijing Weitong Lihua Company (Beijing, China). Certificate number: SCXK (Shanghai 2003-0003).

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Groups: the 45 SHR aged 8 weeks old were randomly divided into group A, group B, and group C. All rats in group A were injected with 3×10^9 infectious unit (IFU) of Profilin-1 overexpressing adenoviral vector of pAd-Profilin-1-RES-EGFP (Shanghai Invitrogen, Shanghai, China) through the tail vein, and injected once every four weeks until 16 weeks of age. All rats in group B were injected with recombinant Fibulin 3 protein solution (Shanghai Invitrogen Co., Ltd., Shanghai, China) once a week through the tail vein, 240 ng/kg (w/w), until 16 weeks of age. All rats in group C were injected with normal saline every week through the tail vein, 1 ml at a time until they were 16 weeks old. All rats were kept in a quiet specific pathogen free (SPF) environment with normal light and feeding, and were kept until 16 weeks of age. After the first measurement of weight and blood pressure, five rats were anesthetized by intraperitoneal injection of 3% sodium pentobarbital (Wuhan Xinxin Jiali Biotechnology Co., Ltd., Wuhan, China) (50 mg/kg) each time and were dissected. The thoracic aorta was removed and stored in liquid nitrogen, and the specimen was examined by Western blot. The study has been reviewed and approved by the Ethical Committee of Yan'an University Affiliated Hospital.

Detection of the Protein Expressions of Profilin-1 and Fibulin-3 by Western Blot Analysis

The protein extracted from the thoracic aorta tissue of each rat was placed in a homogenizer (Shanghai Active Motif Biotechnology Co. Ltd. Cat. No. 40401/40415, Shanghai, China). 300 μL of the lysate was added and the tissue block was gradually removed by grinding until there was no impurities or precipitates in the lysate, and cleavage was on ice for 30 min. After the centrifuge at 14000 r/min for 20 min, we finally took the supernatant as the total cellular protein. The BCA protein was quantified and transferred to a polyvinylidene difluoride membrane on a 6% to 12% sodium dodecyl sulfate polyacrylamide gel. After selecting the corresponding bands according to the protein of interest, the cells were blocked with a concentration of 5% skim milk powder for 2 hours. After washing the membrane, a dilution of 1:1,000 was added to 2 ml of Western primary antibody (Jiangsu Biyuntian Biological Co., Ltd., Jiangsu, China), and was then stored in an environment with a temperature of 4°C overnight. On the second day, the primary antibody was reheated for 30 min before the start of the experiment, and the Western secondary antibody (Jiangsu Biyuntian Biological Co., Ltd., Jiangsu, China) was incubated for 1 h in the same procedure, and the developing solution was exposed to the dark room. The polyvinylidene difluoride film was imaged with Tocan240 automatic gel imaging system (Shanghai Lingcheng Biotechnology Co. Ltd., Shanghai, China), and the results were analyzed by Grayscale using Image LabTM software (Bio-rad, Hercules, CA, USA).

Indices Observation

The overexpression of Profilin-1, Fibulin-3 protein, blood pressure, body weight, vascular wall thickness/cavity ratio in group A, group B, group C, and control group at T0 (8 weeks old), T1 (12 weeks old), T2 (16 weeks old) were recorded.

Statistical Analysis

The statistical analysis was carried out using the Statistical Product and Service Solution SPSS 19.0 software system (IBM Corp., Armonk, NY, USA). The counting data were expressed by [n(%)], and the measurement data were expressed by (x±s). The *t*-test was used for data comparison between both groups, and the analysis of variance (ANOVA) was used for comparison within multiple groups. The LSD-*t* test was used as the post-hoc test. When the *p*-value was less than 0.05, the difference was considered statistically significant.

Results

The Expression Level of Profilin-1 Protein of Rats in Each Group

The expression levels of Profilin-1 protein of rats at T0, T1, and T2 in group A were (0.24±0.02), (0.30±0.06) and (0.40±0.05), respectively. The expression levels of Profilin-1 protein of rats at T0, T1 and T2 in group B were (0.24±0.03), (0.26±0.05) and (0.30±0.07), respectively. The expression levels of Profilin-1 protein of rats at T0, T1, and T2 in group C were (0.24±0.04), (0.26±0.06) and (0.30±0.06), respectively. The expression levels of Profilin-1 protein of rats at T0, T1, and T2 in the control group were (0.18±0.05), (0.18±0.04) and (0.18±0.06), respectively. In the comparison within groups, the expression levels of Profilin-1 protein at T0 to T2 of SHR rats in group A, B, and C showed a gradual increasing trend. The expression level of Profilin-1 protein at T2 of group A was significantly higher than that at T0, and the difference was statistically significant ($p<0.05$). When compared between groups, the expression level of Profilin-1 protein of

rats in the control group was significantly lower than that in the other two groups at different time periods, and the difference was statistically significant (p<0.05). There was no significant difference in the expression of Profilin-1 protein at T0 between group A, group B, and group C (p>0.05). The expression level of Profilin-1 protein of rats at T2 in group A was significantly higher than that in the other two groups. There was no significant difference in the expression level of Fibulin-3 protein between group B and group C at different time periods (p>0.05) (Figure 1).

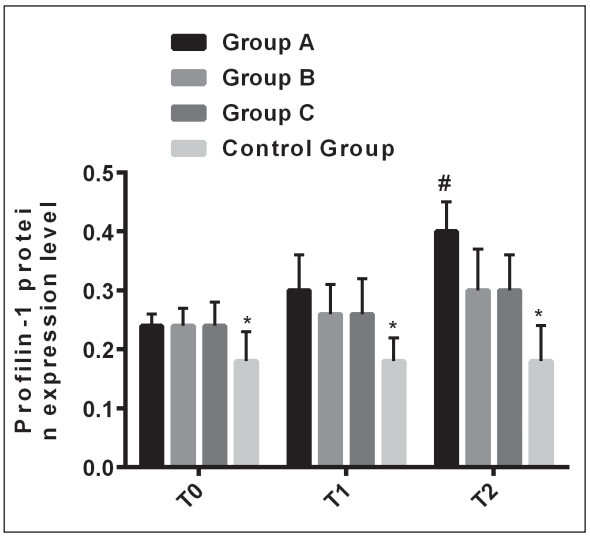

Figure 1. The expression of Profilin-1 in the thoracic aorta of each group was detected by Western blot. The expression levels of Profilin-1 protein in each group were compared within groups, and the expression levels of Profilin-1 protein at T0 to T2 of the two groups of SHR rats gradually increased. The expression level of Profilin-1 protein of rats at T2 in group A was compared with T0, and the difference was statistically significant (p<0.05). In the comparison between groups, the expression level of Profilin-1 protein of rats in the control group was significantly lower than that in the other two groups at different time points, and the difference was statistically significant (p<0.05). The differences in the expression of Profilin-1 protein of rats at T0 between group A, group B, and group C were not statistically significant (p>0.05). The expression level of Profilin-1 protein of rats at T2 in group A was significantly higher than that in the other two groups. There was no significant difference in the expression level of Fibulin-3 protein between group B and group C at different time points (p>0.05).
Note: *indicates that the expression level of Profilin-1 protein of rats in the control group at different time points is significantly lower than that in the other two groups, and the difference is statistically significant (p<0.05); #indicates that the expression level of Profilin-1 protein of rats at T2 in group A is significantly higher than that in the other two groups. The expression level of Profilin-1 protein of rats at T2 in the group is significantly higher than that at T0, and the difference is statistically significant (p<0.05).

The Expression Level of Fibulin-3 of Rats in Each Group

The expression levels of Fibulin-3 protein of rats at T0, T1, and T2 in group A were (0.17±0.05), (0.17±0.06) and (0.18±0.03), respectively. The expression levels of Fibulin-3 protein of rats at T0, T1, and T2 in group B were (0.17±0.06), (0.20±0.04) and (0.24±0.05), respectively. The expression levels of Fibulin-3 protein of rats at T0, T1, and T2 in group C were (0.17±0.04), (0.17±0.07) and (0.18±0.04), respectively. The expression levels of Fibulin-3 protein of rats at T0, T1, and T2 in the control group were (0.11±0.03), (0.11±0.03), and (0.11±0.04), respectively. In the comparison within groups, the expression levels of Fibulin-3 protein at T0 to T2 of the two groups of rats showed a gradual increasing trend, the Fibulin-3 protein expression level at T2 of rats in group B was compared with T0, and the difference was statistically significant (p<0.05). When compared between groups, the expression level of Fibulin-3 protein of rats in the control group was significantly lower than that in the other two groups at different time points, and the difference was statistically significant (p<0.05). There was no significant difference in the expression level of Fibulin-3 protein at T0 between group A, group B, and group C (p>0.05). The expression level of Fibulin-3 protein in group B rats at T2 was significantly higher than that in the other two groups. There was no significant difference in the expression level of Fibulin-3 protein between group A and group C at different time points (p>0.05) (Figure 2).

Comparison of Body Weight of Rats in Each Group

The body weights of rats at T0, T1, and T2 in group A were (197.81±10.25) g, (209.74±9.43) g and (220.81±10.32) g, respectively. The body weights at T0, T1, and T2 in group B were (198.44±11.53) g, (210.25±9.38) g and (221.46±11.63) g, respectively. The body weights at T0, T1, and T2 in group C were (198.86±12.01) g, (210.52±9.96) g and (220.46±10.25) g, respectively. The body weights at T0, T1, and T2 in the control group were (197.61±10.66) g, (209.91±10.42) g and (221.71±10.48) g, respectively. In the comparison within groups, the body weight at T0 to T2 in the two groups of rats showed a gradual increasing trend. Also the body weights of T0, T1, and T2 in each group were statistically significant (p<0.05). When compared between groups, there was no significant difference in the body weight between the groups at different time points (p>0.05) (Table I).

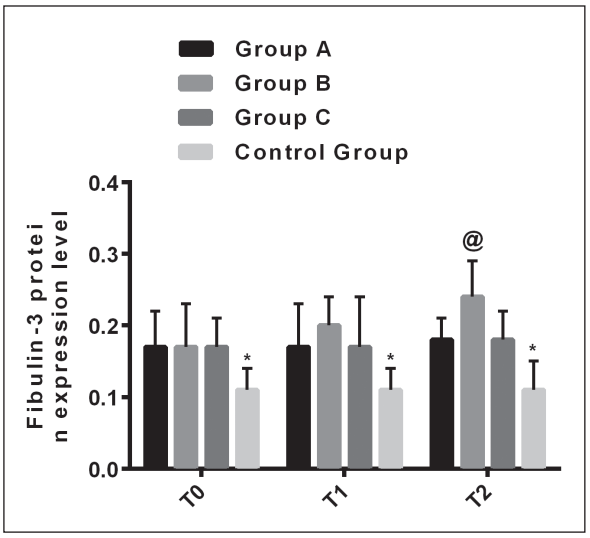

Figure 2. The expression of Fibulin-3 in the thoracic aorta of each group was detected by Western blot. The expression levels of Fibulin-3 protein of rats in each group were compared between groups. The expression level of Fibulin-3 protein of rats in the control group was significantly lower than that in the other two groups at different time points, and the difference was statistically significant (p<0.05). The difference in the expression level of Fibulin-3 protein of rats at T0 between group A, group B, and group C were not statistically significant (p>0.05). The expression level of Fibulin-3 protein of rats in group B at T2 was significantly higher than that in the other two groups. There were statistically significant difference in the expression level of Fibulin-3 protein between group A and group C at different time points (p>0.05).
Note: *indicates that the expression level of Fibulin-3 protein of rats in the control group at different time points is significantly lower than that in the other two groups, the difference is statistically significant (p<0.05); #indicates that the expression level of Fibulin-3 protein of rats at T2 in group B is significantly higher than that in the other two groups. Also, the Fibulin-3 protein expression level of rats at T2 in each group is compared with T0, and the difference is statistically significant (p<0.05).

Comparison of Blood Pressure of Rats in Each Group

The systolic blood pressures of rats at T0, T1, and T2 in group A were (135.29±16.02) mmHg, (151.02±19.36) mmHg and (210.32±16.29) mmHg, respectively. The systolic blood pressures of rats at T0, T1, and T2 in group B were (134.28±15.78) mmHg, (142.24±17.35) mmHg, (152.84±16.25) mmHg, respectively. The systolic blood pressures of rats at T0, T1, and T2 in group C were (135.45±15.24) mmHg, (150.37±20.38) mmHg, (200.46±15.59) mmHg, respectively. The systolic blood pressures of rats at T0, T1, and T2 in the control group were (100.12±12.46) mmHg, (101.45±11.28) mmHg, and (100.98±11.59) mmHg, respectively. When compared within groups, there was no statistically significant difference in the systolic blood pressure of rats at T0, T1, and T2 (p<0.05). The systolic blood pressure at T0 to T2 in group A, group B and group C showed a gradual increasing trend, and the differences of the systolic blood pressure at T0, T1, and T2 in group A and group C were statistically significant (p<0.05). The systolic blood pressure of rats at T2 in group B was compared with T0, and the difference was statistically significant (p<0.05). In the comparison between groups, the systolic blood pressure of rats in the control group at different time points was significantly lower than that of groups A, B, and C, and the difference was statistically significant (p<0.05). There was no significant difference in systolic blood pressure of rats at T0 between group A, group B, and group C (p>0.05). The systolic blood pressure at T2 of group A was significantly higher than that of the other two groups (p<0.05). The systolic blood pressure of rats at T2 in group B was significantly lower than that of group A and group C, and the difference was statistically significant (p<0.05) (Table II).

The thickness of vascular wall of rats in each group

The wall thickness at T0, T1, and T2 in group A was (92.25±7.28) μm, (111.68±10.45) μm, (123.35±10.21) μm, respectively. The wall thickness of rats at T0, T1, and T2 in group B was (91.28±6.51) μm, (110.93±11.28) μm, (122.67±10.35)

Table I. Comparison of body weight of rats in each group.

Groups	Group A	Group B	Group C	The control group	F	p
T0 (n=15)	197.81±10.25	198.44±11.53	198.86±12.01	197.61±10.66	0.041	0.989
T1 (n=10)	209.74±9.43	210.25±9.38	210.52±9.96	209.91±10.42	0.013	0.989
T2 (n=5)	220.81±10.32	221.46±11.63	220.46±10.25	221.71±10.48	0.015	0.989
F	11.200	9.432	8.146	11.700		
p	<0.001	<0.001	0.002	<0.001		
Blood ketones	5.7±0.12	0.09±0.03	25.375	<0.001		

Table II. Comparison of blood pressure (mmHG) of rats in each group.

Groups	Group A	Group B	Group C	The control group	F	p
T0 (n=15)	135.29±16.02*	134.28±15.78	135.45±15.24*	100.12±12.46[@]	20.710	<0.001
T1 (n=10)	151.02±19.36*	142.24±17.35	150.37±20.38*	101.45±11.28[@]	18.210	<0.001
T2 (n=5)	210.32±16.29*	152.84±16.25[#]	200.46±15.59*	100.98±11.59[@]	49.050	<0.001
F	25.370	2.542	26.890	0.039		
p	<0.001	0.097	<0.001	0.962		

Note: *indicates that the difference in systolic blood pressure of rats at different time points is statistically significant ($p<0.05$); [#]indicates that the systolic blood pressure of rats at T2 of the B group was compared with T0, the difference was statistically significant ($p<0.05$); [@]indicates that the systolic blood pressure of rats in the control group at different time points is significantly lower than other groups A, B, and C, the difference is statistically significant ($p<0.05$);

μm, respectively. The wall thickness of rats at T0, T1, and T2 in group C was (92.17±7.05) μm, (95.29±8.14) μm, (102.32±5.89) μm, respectively. The thickness of the vascular wall of rats at T0, T1, and T2 in the control group were (78.28±4.18) μm, (80.55±5.06) μm, (81.45±6.01) μm, respectively. In the comparison within groups, the thickness of the vascular wall of the rats in each group from T0 to T2 showed an increasing trend. The difference of the thickness of the vascular wall at T0, T1, and T2 in group A and group B was statistically significant ($p<0.05$). The thickness of the vascular wall at T2 in group C was significantly higher than that at T0, and the difference was statistically significant ($p<0.05$). When compared between groups, in the control group, the thickness of vascular wall at different time points was significantly lower than that of the other two groups, and the difference was statistically significant ($p<0.05$). There was no significant difference in the thickness of vascular wall of rats at T0 between group A, group B, and group C ($p>0.05$). The thickness of the vascular wall of rats in the control group and group C at T1 and T2 was significantly lower than that of group A and group B, and the thickness of vascular wall of rats in the control group at T1 and T2 was significantly lower than that of group C, with statistically significant difference ($p<0.05$) (Table III).

The Vascular Wall/Cavity Ratio of Rats in Each Group

The vascular wall/cavity ratios at T0, T1, and T2 in group A were (6.04±0.42), (7.78±0.53) and (8.03±0.15), respectively. The vascular wall/cavity ratios at T0, T1, and T2 in group B were (6.06±0.52), (7.56±0.51) and (8.01±0.45), respectively. The vascular wall/cavity ratios at T0, T1, and T2 in group C were (6.06±0.59), (7.48±0.49) and (8.00±0.43), respectively. The vascular wall/cavity ratios at T0, T1, and T2 in the control group were (6.02±0.34), (6.04±0.56) and (6.06±0.58), respectively. In the comparison within groups, the vascular wall/cavity ratio at T0 to T2 in each group of SHR rats showed an increasing trend. There was no significant difference in the vascular wall/cavity ratio at T0, T1, and T2 in the control group ($p>0.05$). The vascular wall/cavity ratios of rats at T2 in group A, group B, and group C were compared with T0, and the difference was statistically significant ($p<0.05$). When compared between groups, there was no significant difference in vascular wall/cavity ratio between the groups at T0 ($p>0.05$). The vascular wall/cavity ratios of the rats in group A, group B, and group C were significantly higher than that in the control group at T1 and T2, and the difference was statistically significant ($p<0.001$). There were no

Table III. The thickness of vascular wall of rats in each group (um).

Groups	Group A	Group B	Group C	The control group	F	p
T0 (n=5)	92.25±7.28*	91.28±6.51*	92.17±7.05	78.28±4.18[@]	6.000	0.006
T1 (n=5)	111.68±10.45*	110.93±11.28*	95.29±8.14	80.55±5.06[@]	13.270	<0.001
T2 (n=5)	123.35±10.21*	122.67±10.35*	102.32±5.89[#]	81.45±6.01[@]	28.040	<0.001
F	13.900	13.630	2.829	0.505		
p	<0.001	<0.001	0.099	0.616		

Note: *indicates the difference of the thickness of vascular wall of rats at T0, T1 and T2 in group A and group B is statistically significant ($p<0.05$). [#]indicates that the thickness of the vascular wall at T2 in group C compared with T0, and the difference is statistically significant ($p<0.05$). [@]indicates that the thickness of vascular wall of rats at different time points in the control group was significantly lower than that in the other groups A, B, and C, and the difference is statistically significant ($p<0.05$).

Table IV. The vascular wall /cavity ratio of rats in each group.

Groups	Group A	Group B	Group C	The control group	*F*	*p*
T0 (n=5)	6.04±0.42	6.06±0.52	6.06±0.59	6.02±0.34	0.008	0.999
T1 (n=5)	7.78±0.53	7.56±0.51	7.48±0.49	6.04±0.56#	11.500	<0.001
T2 (n=5)	8.03±0.15*	8.01±0.45*	8.00±0.43*	6.06±0.58#	25.570	<0.001
F	36.740	21.330	19.570	0.008		
p	<0.001	<0.001	<0.001	0.992		

Note: * indicates the vascular wall/cavity ratio of rats at T2 in group A, group B, and group C is significantly higher than that at T0 ($p<0.05$). # indicates that the vascular wall/cavity ratio of rats in the control group T1 and T2 time is significantly higher than that of group A, group B, and group C, and the difference was statistically significant ($p<0.001$).

significant differences in the vascular wall/cavity ratio between group A, group B, and group C at T1 and T2 ($p>0.05$) (Table IV).

Discussion

Hypertensive vascular remodeling is a very complicated pathological process, in which the dysfunction of vascular endothelium and the changes of various factors in vascular endothelial cells may lead to the occurrence and development of vascular remodeling[10,11]. Reports[12,13] focusing on hypertensive vascular remodeling have found that the expression of Profilin-1 is high in the vascular endothelial dysfunction and vascular endothelial cells, and the vascular remodeling of hypertension and the pathological changes in the aorta can be affected by interfering with or over-expressing the Profilin-1. It has been suggested[14] that Fibulin-3 can be used as a vascular antagonistic factor. However, few investigations focus on the application of the Profilin-1 and Fibulin-3 to hypertensive rats. Thus, the effects of Profilin-1 and Fibulin-3 on the rats with hypertensive vascular remodeling still remain unclear. In order to contribute to future studies regarding the clinical prevention of hypertension vascular remodeling, the present work explored the expressions and roles of Fibulin-3 and Profilin-1 in the process of hypertensive vascular remodeling of rats.

The present analysis recorded the body weight, blood pressure, vessel wall thickness, and vessel wall/cavity ratio of the rats. By comparing the changes in the body weight of each group, we found that the two groups of SHR rats all showed an upward trend between T0 and T2 in body weight, and there was significant differences in the body weight between T0, T1, and T2 for each group. However, there was no significant differences in the body weight between the groups at different time points. Some investigations[15,16] have compared the body weights of SHR rats with those of the normal rats, but with little effect on the research data. Thus, we believe that the overexpression of Profilin-1 and Fibulin-3 proteins would not affect the rats' body weight greatly. By comparing the pre and post expression process of the Profilin-1 and Fibulin-3 proteins of each group of rats, we found that for each group, the expression levels of Profilin-1 and Fibulin-3 all showed an upward trend between T0 and T2. The difference in Profilin-1 protein expression level between T2 and T0 in the group A, and the difference in Fibulin-3 protein expression level between T2 and T0 in the group B are statistically significant. According to the comparisons between the groups, the expression levels of the Profilin-1 and Fibulin-3 protein of the control group at different time points were significantly lower than those of the other two groups. There was no significant difference in expression levels of Profilin-1 and Fibulin-3 at T0 between the group A, group B, and group C. The expression level of Profilin-1 protein of the group A at T2 was significantly higher than that of the other two groups. The expression level of Fibulin-3 protein of group B at T2 was significantly higher than that of the other two groups. The differences in the expression levels of the Fibulin-3 at different time points between group A and group C and between group B and group C both have no statistical significance. Related reports[17,18] have found that the Fibulin-3 is an extracellular matrix protein that can stabilize the extracellular matrix structure. Luong et al[19] found that the Fibulin-3 levels in healthy rats' serum were lower than those in hypertensive rats' serum. The profilin-1 is a key actin binding regulatory protein in cardiovascular tissues, whose level has been proved to be higher in a hypertensive rat than a healthy one[20,21]. This is similar to the finding of

the present study, which shows the difference in the expression levels of the Profilin-1 and Fibulin-3 protein between the SHR rats and the WKY rats. After the respective overexpression of Profilin-1 and Fibulin-3, the systolic blood pressure between T0 and T2 of the each group of SHR rats showed an upward trend, while the systolic blood pressure of the healthy WKY rats at different time points in the control group was significantly lower than each group of SHR rats. In terms of the systolic blood pressure of the SHR rats, group A was significantly higher than the other two groups at T2, and group B was lower than group A and group C at T1 and T2, respectively. As such, it is speculated that both Profilin-1 and Fibulin-3 have a regulatory effect on the blood pressure for a hypertensive rat. In the current study, the overexpression of Profilin-1 of the SHR rats would raise the rate of increase in their systolic blood pressures, while the overexpression of the Profilin-3 would reduce the rate of increase in their systolic blood pressures. The research on the relationships of the Profilin-1, Fibulin-3, and hypertensive rats, or elderly hypertensive patients have showed that Fibulin-3 can reduce the blood pressure of patients with hypertension, and Profilin-1 functions[22,23]. Finally, we observed the vascular wall thickness and vessel wall/cavity ratio of each group and found that the thickness of the vessel wall of each group between T0 and T2 showed an upward trend for each group. The thickness of the vessel wall at different time points in the control group was significantly lower than the other two groups. The thickness of the vessel wall of the control group and group C at T1 and T2 was significantly lower than that of group A and group B. Based on the findings, we believe that the overexpression of the Profilin-1 and the Fibulin-3 would raise the thickening rate in the thoracic aorta wall for a hypertensive rat. However, by observing the vascular wall/cavity ratio of each group of rats, we found that the overexpression of the Profilin-1 and the Fibulin-3 has little effect on the vessel wall/cavity ratio for a hypertensive rat, and there was no statistically significant difference in the vessel wall/cavity ratio between each group of the hypertensive rats. Whereas, there are reports[24-26] suggesting that the thickening of the vessel wall and an increase in the ratio of the vessel wall/cavity are both pathological manifestations that cause hypertensive vascular remodeling. Therefore, in the present work, we revealed that the overexpression of the Profilin-1 and the Fibulin-3 would not increase the vessel wall/cavity ratio for the hypertensive rats, and would not reverse the pathological manifestations of the hypertensive vascular remodeling. Accordingly, the changes in the Profilin-1 and the Fibulin-3 levels are considered to affect the occurrence and development of hypertensive vascular remodeling. In this case, Profilin-1 and the Fibulin-3 can be regarded as sensitive testing indicators for hypertensive vascular remodeling.

In the current analysis, the amount of the rats is not considerable, which may cause the contingency to the results. Thus, this work only seeks to provide a reference for future research. More studies on the relationship of the Profilin-1, the Fibulin-3, and hypertensive vascular remodeling will be conducted in the future, and we will pay close attention to further researches for the improvement of our study.

Conclusions

The changes in the Profilin-1 and Fibulin-3 levels will affect the occurrence and development of hypertensive vascular remodeling, so Profilin-1 and Fibulin-3 can be regarded as sensitive testing indicators for hypertensive vascular remodeling.

Conflict of Interests

The authors declare that they have no conflict of interest.

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