Elastic aortic wrap reduced aortic stiffness by partially alleviating the impairment of cholesterol efflux capacity in pigs

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Abstract

Purpose Metabolic syndrome patients exhibit impaired cholesterol efflux capacity. Previous studies have shown a positive association between aortic stiffness and metabolic syndrome. However, it is unknown whether cholesterol efflux capacity participates in the process of aortic stiffness. This study sought to determine the effect of metabolic syndrome on aortic stiffening, and to investigate the effectiveness of aortic wraps on aortic compliance and the underlying mechanisms.

Methods In a swine model of metabolic syndrome, we compared the cholesterol efflux capacity and aortic compliance responding to diet modifications and aortic wrap applications.

Results Metabolic syndrome induced by high cholesterol diet significantly decreased cholesterol efflux capacity and aortic compliance. Elastic aortic wrap application increased aortic compliance and partially restored cholesterol efflux capacity via ATP binding cassette transporter A1 (ABCA1) pathway.

Conclusions Cholesterol efflux plays a role in aortic stiffening. Elastic aortic wrap application could be a potential treatment for aortic stiffness related to metabolic syndrome.

Keywords Cholesterol efflux capacity · Aortic stiffness · Pigs · Metabolic syndrome · Aortic wrap

Abbreviations

Apo	Apolipoprotein (Apo)
ABCA1	ATP binding cassette transporter A1
ABCG1	ATP binding cassette transporter G1
EF	Ejection fraction
LVEDV	Left ventricular end diastolic volume
LVESV	Left ventricular end systolic volume
PSEM	Pressure-strain elastic modulus
SR-BI	Scavenger receptor class B, type I
TEE	Transesophageal echocardiography

Introduction

Metabolic syndrome is a cluster of dyslipidemia, central obesity, hypertension and insulin resistance, is associated with increased risks for cardiovascular disease and type 2 diabetes mellitus [1]. Previous studies have shown a positive association between aortic stiffness and metabolic syndrome [2–4]. The mechanisms through which metabolic syndrome increases cardiovascular risks may also involve pathophysiological changes in the arterial wall, which lead to an increase stiffness in large arteries [5]. Indeed, metabolic syndrome patients present impaired cholesterol efflux capacity, which is independently associated with the development of atherosclerosis [6]. Three cholesterol transporters, ATP binding cassette (ABC) transporter A1, ABCG1, and scavenger receptor class B type I (SR-BI), have been shown to play important roles in the regulation of cholesterol efflux [7]. ABCA1 facilitates the efflux of free cholesterol to lipid-free apolipoprotein (Apo) A1, the major protein component of high-density lipoprotein (HDL); ABCG1 and SR-BI mediates cholesterol efflux to mature HDL [8]. Increasing evidence is supporting a potential role of cholesterol efflux in aortic stiffness [9]. ABCA1 regulates endothelial function [10, 11], influences vascular smooth

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muscle cell (VSMC) proliferation and behaviour [12], suppresses inflammation [13] and is therefore considered to be the main contributor to arterial stiffness changes.

Aortic stiffness is the rigidity of the aorta and the elastic resistance to deformation during heart contraction. It is believed to be one of the earliest detectable parameters of adverse functional and structural changes within the aortic wall [14] and to be an independent predictor of cardiovascular events and mortality [15, 16]. Although there are a number of strategies to reduce arterial stiffening, no pharmacological treatments have been validated clinically or in a large cohort [17]. Meanwhile, the application of aortic wrap as a potential non-pharmacological treatment is proposed as a simulation modelling study demonstrates that the aortic wrap procedure is able to compensate for the increase in arterial pulse pressure associated with vessel diameter reduction by a decrease in arterial pulse pressure determined by a reduction in functional stiffness of the ascending aortic segment [18]. In the present study, we therefore aimed to determine the effect of a high-cholesterol diet induced metabolic syndrome on aortic stiffness in a swine model, and to investigate the effectiveness of aortic wraps on aortic compliance and the underlying mechanisms.

Methods

This study was performed in accordance with the Guide for the Care and Use of Laboratory Animals published by the US NIH. All protocols were approved by the Animal Ethics Committee of Nanchang University. Male Yorkshire pigs aged 8 weeks old (Nanjing Agricultural University, China) were housed in cages individually under standard conditions and maintained at 16–22 °C and humidity 60–80%. After 5 days of acclimatization to the environment, the animals were randomized into 2 groups: normal diet ($n = 6$) and high cholesterol diet ($n = 24$). The normal diet (ND) group consumed 500 g of a regular chow based on corn and soybean meal daily. Pigs in the high-cholesterol diet (HCD) group were subjected to aortic balloon injury to enforce the development of aortic stiffness. A 3F Fogarty embolectomy catheter (Baxter) was inserted into the right femoral artery, advanced 30 to 35 cm proximally to the ascending aorta. Denudation was then performed by inflating the balloon with normal saline and slowly pulling it back with the feeling of resistance. This procedure was repeated twice. Pigs were thereafter fed with 500 g of a hypercholesterolemic diet consisting of 75% regular chow, 17.2% coconut oil, 4% cholesterol, 2.3% corn oil, and 1.5% sodium citrate for 12 weeks. This diet is known to induce metabolic syndrome characterized by obesity, hypercholesterolemia, insulin resistance and hypertension as previously described [19, 20]. The diet was continued for the duration of the

experiment. After 12 weeks of dietary modification, all animals in ND group and 6 randomly selected animals in HCD group were sedated by an intramuscular injection of a mixture of 0.1 mg/kg midazolam and 8 mg/kg ketamine, followed by endotracheal intubation. General anaesthesia was maintained with a gas mixture of oxygen at 2 L/min and 2% isoflurane. Body mass index (BMI) was calculated by using the weight of the animal and the length (from tip of the snout to the base of the tail along the back). The vital signs were recorded intra-operatively and throughout postoperative recovery. Arterial access and invasive blood pressure monitoring were achieved by carotid artery cannulation. The tip of the catheter was placed in the ascending aorta region guided by transesophageal echocardiography (TEE). TEE guided M-mode images were used to assess systolic and diastolic diameters of the ascending aorta. Left ventricular end diastolic volume (LVEDV), left ventricular end systolic volume (LVESV) and ejection fraction (EF) were determined using the Teichholz formula. Aortic stiffness of the ascending aorta was assessed using the pressure-strain elastic modulus (PSEM) and was calculated using the following formula: $PSEM = [k(sBP - dBP)/(sD - dD/dD)]/10,000$ where $k = 133.3$ is the conversion factor from mmHg to Nm^{-2} (Pascal units), sBP = systolic blood pressure, dBP = diastolic blood pressure, sD = systolic diameter, and dD = diastolic diameter [21]. Intravenous glucose challenge testing was performed to attain blood glucose levels of baseline, 30 min and 1 h post-glucose infusion. After all the measurements were taken, pigs were euthanised. The heart and the ascending aorta was exposed and harvested through a median sternotomy.

12 animals were randomly selected in the HCD group. Under general anaesthesia, the heart was exposed via a left anterolateral thoracotomy. The ascending aorta was dissected from the pulmonary artery and a segmental aortic wrap (4 cm in length), either elastic or non-elastic, was applied to the ascending aorta and fixed in place with a metal clamp. An elastic silicon polymer (Medtronic, Minneapolis, US) was used as the elastic wrap material. A 4% stiffness material was selected, and the internal diameter of the elastic wrap was set towards the mean value of aortic diameter in the ND group, based on the data of a pilot study performed by Iliopoulos aiming to produce a greater reduction in aortic stiffness [22]. A polytetrafluoroethylene material was served as the non-elastic wrap, which has been reported to increase aortic stiffness in a rabbit model of hypertension [23], the internal diameter of the elastic wrap was also set towards the mean value of aortic diameter in the ND group as comparison. LVEDV, LVESV, EF, as well as aortic stiffness of the ascending aorta were assessed by TEE before and after aortic wrap applications. The leftover 6 animals the HCD group served as controls underwent mock surgery without aortic wrap applications. All the animals were euthanised at 2 weeks postoperatively. Blood samples were collected, and serum samples

were stored at -80°C . The aortas were harvested and frozen in liquid nitrogen for further analysis.

Plasma analysis

Serum total cholesterol, low-density lipoprotein (LDL) and HDL measurements were performed by Central Lab, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China. Serum Apo A1 and Apo B were measured by swine-specific enzyme-linked immunosorbent assays (ELISAs) as per the manufacturers' instructions (LifeSpan Biosciences, Seattle, US).

Cholesterol efflux capacity assay

Apo B-depleted serum was prepared by addition of PEG 6000 using the method previously described [24]. Cholesterol efflux capacity assays were performed using human cAMP-treated J774 macrophages and several cellular models: rat hepatoma Fu5AH expressing high levels of SR-BI, Chinese hamster ovary (CHO)-K1, CHO-ABCG1 overexpressing the human ABCG1, and CHO-ABCA1 overexpressing the human ABCA1 as previously described [25–27]. [^3H]-cholesterol-labelled cells were incubated 4 h at 37°C in the presence of 40-fold diluted serum samples. ABCG1-dependent efflux was calculated as the difference between efflux to CHO-ABCG1 and CHO-K1 cells. The ABCA1-dependent efflux was calculated as the difference between efflux to activated CHO-ABCA1 induced by tetracycline ($1\text{ }\mu\text{g/mL}$) and nonactivated cells. Fractional cholesterol efflux was calculated as the amount of the label recovered in the medium divided by the total label in each well. All efflux experiments were performed in triplicate for each sample.

Western blotting

Whole-cell lysates were made from homogenized harvested aorta samples with radio-immunoprecipitation assay buffer (Abcam, Cambridge, UK) containing a protease inhibitor cocktail (Roche, Lewes, UK). Protein concentrations were determined through a Direct Detect Spectrometer (Merck, Darmstadt, Germany). Western blotting was carried out by Simple Western assays as per the manufacturers' instructions (Protein Simple, San Jose, US). Signal and quantitation of immunodetected proteins were generated automatically at the end of the run. Specific antibodies were used to detect the expressions of ABCA1 (NB400–105, Novus Biologicals, Littleton, US), ABCG1 (LS-C313008–100, LSBio, Seattle, US), SR-BI (NB400–104, Novus Biologicals) and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) expression (MAB374, Millipore). All the blots were normalized against the background and with GAPDH protein.

Statistical analysis

All normally distributed data are expressed as means $\pm$ S.E.M and were compared using Student's *t* test, one-way ANOVA with post-hoc analysis (Tukey's procedure). Analysis was conducted using IBM SPSS Statistics 22. A *p*-value of <0.05 was accepted as statistically significant.

Results

Baseline characteristics

All animals survived the entire procedure. There was no significant difference in the BMI between the groups at the beginning of the experiment. The Baseline characteristics after 12 weeks of modified diet are shown in Table 1. The BMI, total cholesterol, LDL and HDL was significantly higher in the HCD group compared to ND group. Despite there were no statistical difference in blood glucose levels between the two groups at baseline and 1 h post-glucose infusion measurements, the HCD group had blood glucose levels at 30 min post-glucose infusion significantly higher than the ND group. In addition, the mean blood pressure, mean aortic diameter, as well as the calculated PSEM were significantly increased in the HCD group. However, the LVEDV, LVESV and EF were not affected by HCD.

Table 1 The characteristic changes after 12 weeks of modified diet

	ND (<i>n</i> = 6)	HCD (<i>n</i> = 6)	<i>p</i> value
BMI, kg/m^3	29.8 ± 2.2	40.2 ± 3.4	0.028
Total cholesterol, mg/dl	69 ± 3	495 ± 5	0.0001
LDL, mg/dl	25 ± 2	331 ± 3	0.0001
HDL, mg/dl	38 ± 3	209 ± 4	0.0001
Apo B, ng/ml	70.5 ± 4.8	110.7 ± 6.6	0.0006
Apo A1, ng/ml	81.5 ± 4.1	90.3 ± 4.9	0.19
Apo B/Apo A1 ratio	0.86 ± 0.04	1.25 ± 0.12	0.012
Baseline blood glucose, mmol/L	5.1 ± 0.8	4.8 ± 1.1	0.83
30 min blood glucose, mmol/L	6.2 ± 0.7	9.3 ± 0.9	0.022
1 h blood glucose, mmol/L	6.8 ± 0.7	7.2 ± 1.8	0.84
Mean blood pressure, mmHg	75 ± 5	96 ± 4	0.014
Mean aortic diameter, cm	1.86 ± 0.12	2.37 ± 0.17	0.034
PSEM, Pascal units	4.4 ± 0.8	7.9 ± 1.1	0.028
LVEDV, ml	37.1 ± 3.1	35.6 ± 4.2	0.78
LVESV, ml	14.3 ± 1.6	13.9 ± 2.3	0.89
EF	55.4 ± 7.6	53.2 ± 5.2	0.82
Total cholesterol efflux capacity	6.45 ± 0.59	9.11 ± 0.58	0.021
ABCA1-dependent efflux capacity	4.58 ± 0.54	7.31 ± 0.25	0.001
ABCG1-dependent efflux capacity	6.75 ± 0.59	9.78 ± 0.52	0.003

Results expressed as mean $\pm$ SEM. Groups were compared using Student's *t* test

Aortic wrap applications

Before aortic wrap applications, there were no differences in the mean blood pressure, mean aortic diameter, PSEM, LVEDV, LVESV and EF between the elastic aortic wrap group and non-elastic aortic wrap group (Table 2). After aortic wrap applications, elastic aortic wrap significantly decreased PSEM. Neither elastic aortic wrap nor non-elastic aortic wrap affected the mean blood pressure, LVEDV, LVESV and EF (Table 2).

Plasm Apo B and Apo A1

The plasma concentrations of Apo B were significantly higher, and the Apo B/Apo A1 ratios were significantly lower in the HCD group than in the ND group (Table 1). However, there were no significant differences in Apo B and Apo A1 concentrations and Apo B/Apo A1 ratio before and after aortic wrap applications (Table 2).

Cholesterol efflux capacity

After 12 weeks of modified diet, total cholesterol efflux capacity was significantly decreased in the HCD group compared to ND group (Table 1). ABCA1-dependent and ABCG1-dependent efflux, in particular, were significantly decreased (Table 1).

After 2 weeks of aortic wrap applications, although total cholesterol efflux capacity was unchanged, ABCA1-dependent efflux was significantly increased in animals under elastic aortic wrap procedures, compared to non-elastic aortic wrap animals or controls in the HCD group (Fig. 1a and b). ABCG1-dependent efflux was increased in animals under elastic aortic wrap procedures, compared to non-elastic aortic wrap animals (Fig. 1c). SR-BI-dependent efflux were not affected by either elastic aortic or non-elastic aortic wrap applications (Fig. 1d).

Aortic cholesterol acceptor/receptor expressions

Western blotting revealed that decreased levels of ABCA1 and ABCG1 and increased SR-BI levels in the aorta of HCD group, compared to ND group (Fig. 2a, b and c). Aortic expression of ABCA1 was significantly increased in animals under elastic aortic wrap procedures, compared to non-elastic aortic wrap animals or controls in the HCD group (Fig. 2a). However, ABCG1 or SR-BI were not affected by aortic wrap applications (Fig. 2b and c).

Discussion

In present study, we developed a swine aortic stiffness model in response to 12 weeks of high cholesterol diet and aortic balloon injury, and also investigated the effect of aortic wrap on this model, in terms of aortic compliance and cholesterol metabolism. After diet modifications, the animals exhibited characteristic features of metabolic syndrome with obesity, hypercholesterolemia, hypertension and glucose intolerance. Increased aortic stiffness was observed in metabolic syndrome induced by high cholesterol diet. Elastic aortic wrap, served as a counterpulsation device, significantly reduced aortic stiffness without immediately changes of the hemodynamic parameters, but significantly affected cholesterol efflux capacity and aortic cholesterol transporter expressions after 2 weeks treatment.

Arterial stiffness is an age-related progressive process that shares consequences of a series of diseases including diabetes mellitus, hypertension, metabolic syndrome, chronic kidney disease and others [28]. It develops from a complex interaction between stable and dynamic changes involving structural and cellular elements of the vessel wall, such as endothelial cells, VSMCs, extracellular matrix, inflammatory responses and other functional elements [29]. In our study, we found that decreased cholesterol efflux capacity in metabolic syndrome animals presented increased aortic stiffness. Consistent with our findings, metabolic syndrome has been shown to be associated with

Table 2 Hemodynamic findings after aortic wrap applications

	Elastic aortic wrap (n = 6)			Non-elastic aortic wrap (n = 6)		
	Before	After	<i>p</i> value	Before	After	<i>p</i> value
Apo B, ng/ml	128.7 ± 10.6	116.7 ± 9.9	0.43	109.9 ± 14.6	121.7 ± 18.6	0.63
Apo A1, ng/ml	76.6 ± 8.9	87.1 ± 11.5	0.49	83.6 ± 6.9	92.5 ± 8.2	0.43
Apo B/Apo A1 ratio	1.48 ± 0.43	1.29 ± 0.33	0.73	1.29 ± 0.32	1.32 ± 0.53	0.96
Mean blood pressure, mmHg	88 ± 3	93 ± 4	0.34	91 ± 4	98 ± 6	0.35
Mean aortic diameter, cm	2.35 ± 0.22	1.97 ± 0.12	0.16	2.43 ± 0.31	2.15 ± 0.17	0.45
PSEM, Pascal units	9.7 ± 1.4	5.2 ± 1.1	0.03	7.8 ± 2.2	∞	–
LVEDV, ml	38.2 ± 3.4	40.3 ± 2.2	0.62	37.5 ± 2.3	43.5 ± 3.6	0.19
LVESV, ml	16.5 ± 2.9	16.8 ± 2.4	0.94	17.2 ± 3.4	20.6 ± 2.4	0.43
EF	51.2 ± 3.1	56.4 ± 5.6	0.44	54.8 ± 2.8	53.4 ± 6.4	0.85

Results expressed as mean ± SEM. Groups were compared using Student's *t* test

Fig. 1 Serum cholesterol efflux capacity after 4 weeks aortic wrap applications. **a** total cholesterol efflux capacity. **b** ABCA1-dependent efflux capacity. ABCA1-dependent efflux was significantly increased in animals under elastic aortic wrap procedures, compared to non-elastic aortic wrap animals or controls in the HCD group. **c** ABCG1-dependent efflux capacity. ABCG1-dependent efflux was increased in

animals under elastic aortic wrap procedures, compared to non-elastic aortic wrap animals. **d** SR-BI-dependent efflux capacity. Bars indicate mean values. Groups were compared using one-way ANOVA with post-hoc analysis (Tukey's procedure). Groups which do not share the same letter are significantly different from each other ($p < 0.05$). EW, elastic aortic wrap; NEW, non-elastic aortic wrap

increased aortic pulse pressure in patients with normal coronary arteries [30] and with increased pulse wave velocity in 9 countries cohorts [3]. In a swine model of metabolic syndrome, the authors observed increased pro-fibrotic and pro-apoptotic activity, as well as increased inflammatory response in the aorta of high-cholesterol feeding animals [20], contributing the process of aortic stiffening. On the other hand, impaired cholesterol capacity had also been shown in metabolic syndrome subjects previously [31]. Gall et al. demonstrated that cholesterol efflux capacity was reduced progressively as a function of the increasing number of coexisting criteria for the metabolic syndrome [6]. Metabolic syndrome patients have impaired HDL-Apo A1 exchange that contributes to reduced capacity of ABCA1-mediated cholesterol efflux [32]. In addition, the capacity of cholesterol efflux has been shown to be inversely associated with intima-media thickness [33]. Impairment of cholesterol efflux induced a loss of VSMC gene expression and an increase in pro-inflammatory marker expression by cultured mouse and human arterial VSMCs [34]. Cholesterol efflux mediated by ABCA1 and ABCG1 preserves endothelial function by triggering a host of signaling events in endothelial cells, leading to reductions in adhesion molecule and inflammatory protein expression [35] and has been proposed to be a likely predictor for endothelial dysfunction [34]. These studies support our finding that reduced cholesterol efflux capacity may be a key contributor to the aortic stiffness developed in metabolic syndrome patients.

The rate-limiting step of cholesterol efflux is the transport of cholesterol and phospholipids to lipid-free Apo by cholesterol transporters, of which the best characterized are the ABCA1, ABCG1 and SR-BI [7]. Transgenic animals with endothelial-specific overexpression of either ABCA1 or ABCG1 were found to have enhanced cholesterol efflux, attenuated endothelial dysfunction and reduced diet-induced aortic lesion [10, 36]. ABCA1 has been implicated in expression of cyclooxygenase-2 (COX-2) and the release of prostaglandin in endothelial cells [37]. ABCA1 mutation carriers are characterized by increased intima-media thickness [38, 39], while ABCA1-dependent cholesterol efflux is inversely correlated with pulse wave velocity in healthy subjects [40]. In addition, ABCA1 expression plays a critical regulatory role in VSMC differentiation and switch of VSMCs phenotype from contractile to synthetic form [12, 41]. Recent studies also revealed that ABCA1 can function as an anti-inflammatory receptor to suppress the expression of inflammatory factors. ABCA1 deficient mice have increased inflammatory cell infiltration in the vessel wall and the blood stream [42]. The interaction of Apo A1 with ABCA1-expressing macrophages suppressed the induction of the inflammatory cytokines Interleukin (IL)-1 β , IL-6, and tumour necrosis factor (TNF)- α [43]. ABCA1 gene polymorphisms is associated with

Fig. 2 Aortic cholesterol acceptor/receptor expressions. **a** ABCA1 expression. There are significantly decreased levels of ABCA1 in the aorta of HCD group, compared to ND group. Aortic expression of ABCA1 was significantly increased in animals under elastic aortic wrap procedures, compared to non-elastic aortic wrap animals or controls in the HCD group. **b** ABCG1 expression. **c** SR-BI expression. ABCG1

expression was decreased while SR-BI expression was increased after high cholesterol diet treatments. **d** immunoblots of the corresponding proteins. Bars indicate mean values. Groups were compared using one-way ANOVA with post-hoc analysis (Tukey's procedure). Groups which do not share the same letter are significantly different from each other ($p < 0.05$). EW, elastic aortic wrap; NEW, non-elastic aortic wrap

dyslipidemia and production of IL-6 and C-reactive protein (CRP) [44]. The transcription levels of ABCA1 are negatively associated with plasma CRP in Chinese populations [45]. We found that total cholesterol efflux capacity, as well as ABCA1-dependent and ABCG1-dependent efflux was significantly decreased in aortic stiffness models, providing further evidence for the role of cholesterol efflux in aortic stiffening.

Interestingly, we found that reduced aortic stiffness by elastic aortic wrap application significantly increased cholesterol efflux capacity via ABCA1 pathway. Indeed, some previous studies have suggested that the possibility of hemodynamic features changes caused by aortic stiffness may impact on cholesterol efflux [46–50]. In hypertensive patients, the gene expression levels of ABCA1 and ABCG1 in monocytes were negatively associated with blood pressure, and the reduction of ABCA1 and ABCG1 could be reversed by anti-hypertensive therapy [46]. In present study, we also observed decreased aortic ABCA1 and ABCG1 protein levels in hypertensive pigs treated by high-cholesterol diet compared with pigs fed by normal diet. However, elastic aortic wrap application significantly increased aortic ABCA1 levels without affecting blood pressure, suggesting that hemodynamic

changes, not only blood pressure, may play a key role in ABCA1 expression. Peroxisome proliferator-activated receptor gamma ($\text{PPAR}\gamma$)-liver x receptor (LXR)-ABCA1 pathway is one of key pathways in cholesterol efflux in macrophages [47]. It has been reported that decreased $\text{PPAR}\gamma$ gene and protein expression in the lung vascular tissue from pulmonary hypertension patients and rats, whereas high fluid shear stress decreased $\text{PPAR}\gamma$ expression in vitro [48], which potentially impair cholesterol efflux from macrophages. The protein level of LXR and its target ABCA1 in the mouse thoracic aorta was higher than that in the aortic arch, suggesting the mechanism that shear stress regulates LXR expression and impacts on cholesterol efflux [50]. Moreover, reduced cholesterol efflux capacity was also observed in a minipig model of non-ischemic heart failure sustained by high-rate left ventricle pacing, although the hemodynamic changes cannot fully represent the situation in aortic stiffness subjects [49].

Although elevated LDL and decreased HDL levels are currently still mainly used in clinical risk evaluation, accumulating evidence suggests that Apo B and Apo A1 could be better markers of cardiovascular risk [51–53]. Apo A1 is the major protein component of HDL and is

essential for HDL biogenesis and function and plays a fundamental role in the first step of cholesterol efflux [54]. Apo B, on the other hand, is the principal protein component of triacylglyceride and assists the assembly and stability of LDL and its cellular uptake in humans [55]. In present study, we found that increased Apo B/Apo A1 ratio in animal with increased aortic stiffness. Consistent with the report by Kim et al. that Apo B/Apo A1 ratio is independently associated with increased arterial stiffness in patients with metabolic syndrome [56].

Conclusions

This is the first study, to our knowledge, to investigate the effects of aortic stiffness changes by aortic wrap on cholesterol efflux in a swine model of metabolic syndrome. In conclusion, reduced cholesterol efflux in metabolic syndrome is associated with the development of aortic stiffening; elastic aortic wrap can reduce aortic stiffness thereby partial restore the capacity of cholesterol efflux via ABCA1 pathway. Our findings suggest that elastic aortic wrap application is a potential treatment for aortic stiffness, especially in impaired cholesterol efflux patients.

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Compliance with ethical standards

The study protocol was approved by the Animal Ethics Committee of Nanchang University.

Conflict of interest The authors declare that they have no conflict of interest.

Disclosures All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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