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Conference Abstract

P.57 Acetylsalicylic Acid Reduces Passive Aortic Wall Stiffness and Cardiac Remodelling in a Mouse Model of Advanced Atherosclerosis

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Keywords

Aspirin
fibrosis
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ABSTRACT

Background: Acetylsalicylic acid (ASA) is used in secondary prevention of cardiovascular disease (CVD) because of its antithrombotic effects. We investigated whether ASA has additional therapeutic value by preventing the progression of inflammation and cardiovascular remodelling in mice with stable atherosclerosis (*ApoE*$^{-/-}$) and in a model of arterial stiffness with advanced unstable atherosclerotic plaques (*ApoE*$^{-/-}$*Fbn1*$^{C1039G+/-}$ mice).

Methods: Female *ApoE*$^{-/-}$ and *ApoE*$^{-/-}$*Fbn1*$^{C1039G+/-}$ mice were fed a Western diet (WD). At 10 weeks WD, the mice were divided in 2 groups receiving ASA (5 mg/kg/day) via the drinking water or plain water (control) for a period of 15 weeks. Echocardiograms were performed at 10, 17 and 25 weeks WD. At the end, blood pressure was measured via tail-cuff and blood samples were taken. The aorta and heart were collected for histology.

Results: *ApoE*$^{-/-}$*Fbn1*$^{C1039G+/-}$ mice showed an increased neutrophil-lymphocyte ratio (NLR), an important inflammatory biomarker, which was decreased by ASA treatment (Table 1). Wall thickness of the proximal ascending aorta was reduced and elastin/collagen ratio was increased in ASA-treated *ApoE*$^{-/-}$*Fbn1*$^{C1039G+/-}$ mice, resembling values measured in *ApoE*$^{-/-}$ mice (Table 1). Systolic blood pressure, cardiac fibrosis and hypertrophy (Table 1, Figure 1) were reduced after ASA treatment in *ApoE*$^{-/-}$*Fbn1*$^{C1039G+/-}$ mice.

Conclusion: We showed that ASA is able to decrease the NLR, passive aortic wall stiffness and cardiac remodelling in mice with advanced atherosclerosis to levels observed in mice with smaller and more stable atherosclerotic plaques. These data point towards an additional benefit of ASA in the prevention of CVD beyond its classical use.

Table 1 | Summary of main results

	ApoE$^{-/-}$				*ApoE*$^{-/-}$*Fbn1*$^{C1039G+/-}$			
	Control		ASA		Control		ASA	
	Mean ± SEM	N	Mean ± SEM	N	Mean ± SEM	N	Mean ± SEM	N
Blood								
Neutrophils (%)	10.7 ± 2.1	15	9.1 ± 1.5	12	26.4 ± 6.2**	10	13.2 ± 2.1§	7
Lymphocytes (%)	79.2 ± 3.0	15	80.0 ± 4.3	13	58.2 ± 7.9**	10	86.4 ± 2.4§§	7
NLR	0.12 ± 0.02	14	0.12 ± 0.02	12	0.45 ± 0.13***	9	0.16 ± 0.03§§	7
Proximal aorta								
Wall thickness (μm)	64.9 ± 1.5	9	61.7 ± 1.8	10	70.0 ± 2.4	13	60.3 ± 2.9§§	15
Elastin wall (%)	24.1 ± 1.2	9	28.0 ± 1.2	10	19.9 ± 1.1*	13	22.8 ± 1.5	15
Collagen wall (%)	44.4 ± 4.5	9	39.4 ± 3.2	10	63.9 ± 3.9**	13	47.1 ± 3.3§§	15
Elastin/collagen ratio (%)	58.8 ± 5.9	9	75.1 ± 6.9*	10	32.5 ± 2.6***	13	49.5 ± 2.1§§§	15
Heart								
Heart weight/body weight (%)	0.50 ± 0.02	15	0.49 ± 0.02	14	1.16 ± 0.12***	10	0.76 ± 0.05§§§	8
Total fibrosis (%)	5.7 ± 0.2	15	6.1 ± 0.4	14	9.0 ± 0.7***	16	6.1 ± 0.5§§§	15
BP								
Systolic BP (mmHg)	88 ± 4	15	80 ± 4	12	83 ± 6	7	67 ± 4§	8
Diastolic BP (mmHg)	63 ± 4	15	56 ± 3	12	59 ± 6	7	47 ± 4	8

2-way ANOVA followed by a simple main effects analysis including a Bonferroni correction for multiple comparisons: $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$ vs. *ApoE*$^{-/-}$ control and $^{\S}p < 0.05$, $^{\S\S}p < 0.01$, $^{\S\S\S}p < 0.001$ vs. *ApoE*$^{-/-}$*Fbnl* $^{C1039G+/-}$ control. NLR, neutrophillymphocyte ratio; BP, blood pressure.

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