

Supplementary Material for
A Randomized Crossover Air Purifier Intervention Study of
Patients with Stable Coronary Artery Disease

**Zhe Liu¹, Qin Wang¹, Na Li¹, Chunyu Xu¹, Yunpu Li¹, Jun Zhou¹, Liu Liu^{1,2},
Haijing Zhang¹, Yang Mo¹, Dongqun Xu^{1*}**

¹ China CDC Key Laboratory of Environment and Population Health, National Institute of Environmental Health, Chinese Center for Disease Control and Prevention, Beijing 100021, China

² Chaoyang District Center for Disease Control and Prevention, Beijing 100021, China

*Corresponding author: Dongqun Xu

Email: xudq@chinacdc.cn

Table S1 The literature review on the effect of statins on the indicators

ID	Drug names	Subjects	Indicators	Change	Medication Duration	Sample Size (n)	Age	References	Design
1	Atorvastatin	Patients with undergoing coronary artery surgery	IL-6	↓	3W	29:28	61.3±7.7:61.8±7.4	Vukovic et al. 2010	case-control
2	Atorvastatin	Patients with hyperlipidemia	TNF- α IL-6	↓ ↓	8W	45	50±2 (18-71)	Ascer et al. 2004	pre- and post-control
3	Rosuvastatin	Patients with hypertension complicated with dyslipidemia	IL-6 TNF- α CHO LDL-C TG HDL-C	↓ ↓ ↓ ↓ ↓ ↓	12W	16:14	56±8.8:54±8.01	Gómez-García et al. 2007	case-control
4	Atorvastatin	Patients with unstable angina	CRP	↓	16W	2322	—	Kinlav et al. 2002	pre- and post-control
5	Atorvastatin	Patients with SCAD & high SCAD risk	CRP	↓	1M/3M	155	—	Riesen et al. 2002	pre- and post-control
6	Atorvastatin	Patients with CAD	CHO HDL-C LDL-C TG ICAM-1 CD62P	↓ ↑ ↓ ↓ ↓ ↓	12M	28	—	Seljeftot et al. 2002	pre- and post-control

ID	Drug names	Subjects	Indicators	Change	Medication Duration	Sample Size (n)	Age	References	Design
6	Simvastatin	Patients with CAD	CHO HDL-C LDL-C TG ICAM-1 CD62P	↓ ↑ ↓ ↓ ↓ ↓	12M	30	—	Seljeftot et al. 2002	pre- and post-control
7	Simvastatin	Patients with hyperlipidemia	IL-6 sCD62P sCD40L	↓ ↓ ↓	2M	25:20	59±13:55±11	Barale et al. 2018	case-control
8	Atorvastatin	Patients with hyperlipidemia	sCD40L	↓	4W	32	60.3±13.2	Chu et al. 2006	pre- and post-control
9	Simvastatin	Patients with SCAD	ET-1	↓	2W	16	—	Li et al. 2005a	pre- and post-control
10	Pravastatin	Patients with hypertension complicated with dyslipidemia	ET-1	↓	16W	25	53±2	Glorioso et al. 1999	pre- and post-control
11	Atorvastatin	Patients with SCAD	FIB	↓	12W	36	53±9	Atalar et al. 2002	pre- and post-control
12	Fluvastatin	Patients with CAD complicated with dyslipidemia	FIB	↓	24W	82:86	57±8:56±8	Cortellaro et al. 2000	case-control

ID	Drug names	Subjects	Indicators	Change	Medication Duration	Sample Size (n)	Age	References	Design
13	Atorvastatin	Patients with hyperlipidemia	hsCRP	↓	12W	34	59.2±9.3	Qu et al. 2009	pre- and post-control
	MMP-9		↓						
			PAI-1	↓					
	Rosuvastatin	Patients with hyperlipidemia	hsCRP	↓	12W	35	57.7±11.1		
			MMP-9	↓					
			PAI-1	↓					
14	Simvastatin	Patients with CAD complicated with dyslipidemia	MMP-9	↓	14W	13	67±8	Koh et al. 2001	pre- and post-control
			PAI-1	↓					
15	Simvastatin	Patients with CAD complicated with dyslipidemia	CRP	↓	14W	32:31	62±7:62±8	Koh et al. 2002	case-control
			TNF- α	↓					
			MMP-9	↓					
			TIMP-1	↓					
16	Rosuvastatin	Patients with CHF	MMP-2	↓	1M	—	—	Tousoulis et al. 2010	pre- and post-control
			MMP-9	↓		—	—		
17	Pravastatin	Patients with CAD	MMP-2	↓	2M	24	68±2	Fujiwara et al. 2008	pre- and post-control
18	Simvastatin	Patients with CAD complicated with dyslipidemia	MMP-9	↓	8W	27	53	Koh et al. 2004	pre- and post-control
			TIMP-1	↓					

ID	Drug names	Subjects	Indicators	Change	Medication Duration	Sample Size (n)	Age	References	Design
19	Atorvastatin	Patients with hyperlipidemia (64% with CAD)	LDL-C	↓	6W	639	61.7(18-80)	Karalis et al. 2002	pre- and post-control
			TG	↓					
			CHO	↓					
			HDL-C	↑					
	Simvastatin	Patients with hyperlipidemia (63% with CAD)	LDL-C	↓	6W	641	61.5(18-80)		
			TG	↓					
			CHO	↓					
			HDL-C	↑					
Simvastatin	Patients with hyperlipidemia (62% with CAD)	LDL-C	↓	6W	207	61.3(18-80)			
		TG	↓						
		CHO	↓						
		HDL-C	↑						
Simvastatin	Patients with hyperlipidemia (67% with CAD)	LDL-C	↓	6W	207	61.5(18-80)			
		TG	↓						
		CHO	↓						
		HDL-C	↑						

Table S2 The literature review on the effect of β -blockers on the indicators

ID	Drug names	Subjects	Indicators	Change	Medication Duration	Sample Size (n)	Age	References	Design
1	Metoprolol	Patients with CHF	IL-6 TNF- α	↓ ↓	6M	48	61±12	Li et al. 2005b	pre- and post-control
2	Metoprolol/Bisoprolol	Patients with IDCM	TNF- α	↓	12W	32	61 (26-74)	Ohtsuka et al. 2001	pre- and post-control
3	Propranolol/Atenolol/ Metoprolol/Carvedilol	Patients with unstable angina	CRP	↓ ↓ ↓ ↓	admitted to hospital 24H 48H out of the hospital	20:30	60±11: 60±10	Doo et al. 2001	case-control
			IL-6	↓ ↓	admitted to hospital 24H	20:30	60±11: 60±10		
4	Nebivolol	Patients with hypertension	hsCRP	↓	12W	15	—	Rizos et al. 2003	pre- and post-control
	Atenolol	Patients with hypertension	hsCRP CHO	↓ ↓	12W	15	— —		
5	Atenolol	Patients with high risk of CAD	ET-1	↓	4W	22	—	Seljeflot et al. 1999	pre- and post-control
6	Carvedilol	Patients with hypertension	ET-1	↓	3M	35	66.3±4.7	Dong and Yang 2012	pre- and post-control

ID	Drug names	Subjects	Indicators	Change	Medication Duration	Sample Size (n)	Age	References	Design
7	Atenolol	Patients with hypertension	FIB	↓	6M	26	40~65	Makris et al. 2000	pre- and post-control
8	Celiprolol	Patients with hypertension	FIB CHO LDL-C TG	↓ ↓ ↓ ↓	12M	12	39.8	Herrmann and Mayer 1988	pre- and post-control
9	Nebivolol	Patients with hypertension	CHO TG	↓ ↓	6W	6376	>65	Fallois and Faulhaber 2001	pre- and post-control
10	Nebivolol	Patients with hypertension	CHO LDL-C	↓ ↓	12W	26	51.5±10.4	Lacourcière et al. 1992	pre- and post-control

Table S3 The literature review on the effect of Ca-channel blockers on the indicators

ID	Drug names	Subjects	Indicators	Change	Medication Duration	Sample Size (n)	Age	References	Design
1	Nifedipine	DBA/2 mice inoculated with encephalomyocarditis virus	IL-6 TNF- α MMP-2 MMP-9	↓ ↓ ↓ ↓	5D	10:10	4 W	Liu et al. 2009	case-control
2	Barnidipine	Patients with hypertension	IL-6 TNF- α hsCRP	↓ ↓ ↓	6M	149	—	Derosa et al. 2015	pre- and post-control
3	Nifedipine	Patients with hypertension	TNF- α CRP	↓ ↓	12W	83	63.02±2.15	Jiang and Wang 2019	pre- and post-control
4	Lercanidipine	Patients with hypertension	MMP-9	↓	15D	7	48.9±5.3	Martinez et al. 2006	pre- and post-control
5	Barnidipine	Patients with hypertension	hsCRP TNF- α MMP-2 MMP-9	↓ ↓ ↓ ↓	6M	75	60.5±8.9	Derosa et al. 2016	pre- and post-control
	Lercanidipine	Patients with hypertension	MMP-2 MMP-9	↓ ↓	6M	76	60.7±8.8		

Table S4 The literature review on the effect of Clopidogrel on the indicators

ID	Drug names	Subjects	Indicators	Change	Medication Duration	Sample Size (n)	Age	References	Design
1	Clopidogrel	Patients with ACS	TNF- α hsCRP	↓ ↓	30D	57:58	53.5±14.9:52.5±16.9	Chen et al. 2006	case-control
2	Clopidogrel	Patients with SCAD	TNF- α	↓	1Y	101	61(52,79)	Seljeflot et al. 2017	pre- and post-control
3	Clopidogrel	Patients with SCAD	hsCRP CD40L	↓ ↓	5W	77:26	64±4:65±3	Heitzer et al. 2006	case-control
4	Clopidogrel	Patients with SCAD	CD40L	↓	8W	37:36	64±11:66±8	Azar et al. 2006	case-control
5	Clopidogrel	Patients with CAD	CD62P	↓	>3M	8:17	72(50-81):71(46-88)	Klinkhardt et al. 2003	case-control
6	Clopidogrel	Patients with ACS	sCD40L sCD62P	↓ ↓	24H	23	58±10	Xiao and Theroux 2004	pre- and post-control
7	Clopidogrel	Patients with unstable angina	MMP-2 MMP-9	↓ ↓	4W	35	64.2±6.7	Xu and Chen 2013	case-control
8	Clopidogrel	Patients with ischemic stroke	MMP-9	↓	4W	35:35	64.1±7.1:63.7±6.7	Zhang and Ding 2013	case-control
9	Clopidogrel	Patients with ischemic stroke	MMP-9	↓	2W	37	68.1±7.8	Zhang et al. 2013	pre- and post-control
10	Clopidogrel	Mice with AMI	TNF- α MMP-2 MMP-9	↓ ↓ ↓	8W	10:10	—	Korish 2020	case-control

Table S5 The literature review on the effect of Aspirin on the indicators

ID	Drug names	Subjects	Indicators	Change	Medication Duration	Sample Size (n)	Age	References	Design
1	Aspirin	Patients with chronic stable angina	IL-6 CRP	↓ ↓	3W	40	55±5	Ikonomidis et al. 1999	pre- and post-control
2	Aspirin	Patients with angina	IL-6 TNF- α hsCRP	↓ ↓ ↓	4W	30	47.32±5.54	Wang et al. 2017	pre- and post-control
3	Aspirin	Patients with angina	TNF- α hsCRP CHO	↓ ↓ ↓	4W	40	—	Yin 2018	pre- and post-control
4	Aspirin	Patients with hypertension	sCD62P	↓	3M	35	64±7	Nadar et al. 2006	pre- and post-control
5	Aspirin	Patients with CAD	CD62P	↓	2W	41	—	Hou et al. 2010	pre- and post-control
6	Aspirin	Patients with angina	NO	↑	—	30	58.4±8.2	Zhai et al. 2005	case-control
7	Aspirin	Patients with SCAD	NO	↑	12W	37	64	Hetzel et al. 2013	pre- and post-control
8	Aspirin	Patients with unstable angina	CHO LDL-C	↓ ↓	4W	46	53.03±8.67	Su 2017	pre- and post-control
9	Aspirin	New Zealand rabbits with hyperlipidemia atherosclerotic	CHO LDL-C	↓ ↓	4W	—	—	Hua et al. 2009	pre- and post-control

Table S6 The literature review on the effect of ACEI/ARB on the indicators

ID	Drug names	Subjects	Indicators	Change	Medication Duration	Sample Size (n)	Age	References	Design
1	Irbesartan	Patients with CAD complicated with arterial hypertension	IL-6	↓	3M	21	56±8	Schieffer et al. 2004	pre- and post-control
	hsCRP		↓						
			MMP-9	↓					
	Enalapril	Patients with CAD complicated with arterial hypertension	MMP-9	↓	3M	21	56±8		
2	Candesartan	Patients with congestive heart failure	IL-6	↓	14W	44	55.6±3.3	Tsutamoto et al. 2000	pre- and post-control
			TNF- α	↓					
			sICAM-1	↓					
3	Losartan	Patients with hypertension	TNF- α	↓	3M	16	42±4	Cottone et al. 1998	pre- and post-control
			TNF- α	↓	6M	16	42±4		
4	Ramipril	Patients with high cardiovascular risk	hsCRP	↓	6M	77	60±11	Lopez Santi et al. 2005	pre- and post-control
5	Ramipril	SD rats with hypercholesterolemia	ICAM-1	↓	10W	10:10	—	Li et al. 2003	pre- and post-control
	Losartan	SD rats with hypercholesterolemia	ICAM-1	↓	10W	10:10	—		
6	Irbesartan	Patients with hypertension	FIB	↓	6M	28	40~65	Makris et al. 2000	pre- and post-control
7	Perindopril	Patients with hypertension	FIB	↓	6W	28	43-64	Fogari et al. 1998	pre- and post-control

ID	Drug names	Subjects	Indicators	Change	Medication Duration	Sample Size (n)	Age	References	Design
8	Candesartan	Patients with hypertension	MMP-9	↓	3M	17	47±8	Onal et al. 2009	pre- and post-control
	Lisinopril	Patients with hypertension	MMP-9	↓	3M	16	47±8		

Table S7 Analysis model of each indicator and the interpretation contribution rate of its variables to the model

	Models	%change of IQR	95%CI	p-value	AIC	Variables	R ²	Contribution
IL-6	log (Indicator) ~ PM _{2.5} +Age+Gender+BMI+ED ^a +(1 ID)	1.74	(-20.72,29.82)	0.891	135.75	Model	0.110	
						ED	0.074	67.27%
						Age	0.052	47.27%
						BMI	0.009	8.18%
						Gender	0.001	0.91%
						PM _{2.5}	<0.001	<0.01%
TNF- α	log (Indicator) ~ PM _{2.5} +Age+Gender+BMI+ED+(1 ID)	-2.57	(-7.33,2.31)	0.293	51.36	Model	0.098	
						Gender	0.057	58.16%
						Age	0.029	29.59%
						ED	0.008	8.16%
						PM _{2.5}	0.002	2.04%
						BMI	<0.001	<0.01%
CRP	log (Indicator) ~ PM _{2.5} +Gender+BMI+Temp ^b +ED+(1 ID)	-23.43	(-39.03, -3.62)	0.027	127.5	Model	0.143	
						PM _{2.5}	0.078	54.55%
						ED	0.076	53.15%
						Temp	0.018	12.59%
						BMI	0.015	10.49%
						Gender	<0.001	<0.01%

Models		%change of IQR	95%CI	p-value	AIC	Variables	R ²	Contribution
FIB	log (Indicator) ~ PM _{2.5} +Age+Gender+BMI+ED+(1 ID)	-2.81	(-8.90,2.94)	0.37	30.71	Model	0.234	
						Age	0.142	60.68%
						BMI	0.078	33.33%
						Gender	0.073	31.20%
						ED	0.036	15.38%
						PM _{2.5}	0.016	6.84%
CD62P	log (Indicator) ~ PM _{2.5} +Gender+BMI+Temp+ED+(1 ID)	-1.14	(-5.61,4.42)	0.649	23.5	Model	0.194	
						BMI	0.153	78.87%
						ED	0.044	22.68%
						PM _{2.5}	0.002	1.03%
						Temp	<0.001	<0.01%
						Gender	<0.001	<0.01%
CD40L	log (Indicator) ~ PM _{2.5} +Gender+BMI+Temp+ED+(1 ID)	1.76	(-7.24,16.36)	0.728	65.41	Model	0.060	
						Temp	0.044	73.33%
						PM _{2.5}	0.002	3.33%
						ED	0.001	1.67%
						Gender	<0.001	<0.01%
						BMI	<0.001	<0.01%

Models		%change of IQR	95%CI	p-value	AIC	Variables	R ²	Contribution
ICAM-1	log (Indicator) ~ PM _{2.5} +Age+Gender+BMI+ED+(1 ID)	-1.18	(-3.60,1.28)	0.335	27.73	Model	0.204	
						BMI	0.184	90.20%
						ED	0.038	18.63%
						Age	0.027	13.24%
						Gender	0.021	10.29%
						PM _{2.5}	<0.001	<0.01%
NO	log (Indicator) ~ PM _{2.5} +Gender+BMI+Temp+ED+(1 ID)	-10.31	(-25.49,10.42)	0.284	115.94	Model	0.153	
						Gender	0.066	43.14%
						Temp	0.042	27.45%
						BMI	0.031	20.26%
						PM _{2.5}	0.022	14.38%
						ED	0.008	5.23%
ET-1	log (Indicator) ~ PM _{2.5} +Age+Gender+BMI+ED+(1 ID)	-6.2	(-12.98,0.82)	0.082	81.94	Model	0.144	
						Gender	0.096	66.67%
						Age	0.068	47.22%
						ED	0.021	14.58%
						BMI	0.013	9.03%
						PM _{2.5}	0.005	3.47%

Models		%change of IQR	95%CI	p-value	AIC	Variables	R ²	Contribution
MMP-2	log (Indicator) ~ PM _{2.5} +Age+Gender+BMI+ED+(1 ID)	3.9	(-0.91,8.44)	0.097	11.58	Model	0.058	
						PM _{2.5}	0.035	60.34%
						Age	0.021	36.21%
						BMI	0.007	12.07%
						ED	0.002	3.45%
						Gender	<0.001	<0.01%
MMP-9	log (Indicator) ~ PM _{2.5} +Gender+Temp+RH ^c +ED+(1 ID)	-4.59	(-14.90,7.48)	0.448	83.04	Model	0.261	
						Gender	0.153	58.62%
						RH	0.148	56.70%
						Temp	0.075	28.74%
						ED	0.037	14.18%
						PM _{2.5}	0.012	4.60%
TIMP-1	log (Indicator) ~ PM _{2.5} +Gender+Temp+RH+ED+(1 ID)	-1.83	(-4.11,0.52)	0.135	-18.04	Model	0.115	
						RH	0.046	40.00%
						Gender	0.041	35.65%
						Temp	0.039	33.91%
						PM _{2.5}	0.011	9.57%
						ED	0.003	2.61%

	Models	%change of IQR	95%CI	p-value	AIC	Variables	R ²	Contribution
CHO	log (Indicator) ~ PM _{2.5} +Age+Gender+BMI+ED+(1 ID)	3.66	(-0.75,8.85)	0.129	12.74	Model	0.494	
						Gender	0.342	69.23%
						ED	0.126	25.51%
						BMI	0.105	21.26%
						PM _{2.5}	0.033	6.68%
						Age	0.001	0.20%
TG	log (Indicator) ~ PM _{2.5} +Age+Gender+BMI+ED+(1 ID)	-2.34	(-9.96,6.71)	0.583	67.26	Model	0.336	
						ED	0.196	58.33%
						BMI	0.176	52.38%
						Gender	0.162	48.21%
						Age	0.004	1.19%
						PM _{2.5}	0.002	0.60%
HDL-C	log (Indicator) ~ PM _{2.5} +Age+Gender+BMI+ED+(1 ID)	4.09	(-0.08,8.39)	0.05	21.68	Model	0.144	
						Gender	0.063	43.75%
						Age	0.026	18.06%
						PM _{2.5}	0.013	9.03%
						ED	0.003	2.08%
						BMI	<0.001	<0.01%

Models		%change of IQR	95%CI	p-value	AIC	Variables	R ²	Contribution
LDL-C	log (Indicator) ~ PM _{2.5} +Age+Gender+BMI+ED+(1 ID)	7.21	(0.09,17.92)	0.075	47.03	Model	0.314	
						Gender	0.215	68.47%
						BMI	0.083	26.43%
						PM _{2.5}	0.059	18.79%
						ED	0.016	5.10%
						Age	<0.001	<0.01%
Models		β	95%CI	p-value	AIC	Variables	R ²	Contribution
AIP	Index ~ PM _{2.5} +Age+Gender+BMI+ED+(1 ID)	-0.001 ^d	(-0.003,0.001)	0.226	23.35	Model	0.340	
						ED	0.253	74.41%
						BMI	0.140	41.18%
						Gender	0.054	15.88%
						Age	0.012	3.53%
						PM _{2.5}	0.010	2.94%

^a ED: effective drug

^b Temp: Temperature

^c RH: relative humidity;

^d AIP is normally distributed, so there is no need for logarithmic conversion. Therefore, there result shows the correlation coefficient β of PM_{2.5} instead of percentage change associated with a PM_{2.5} interquartile range decrease.

References S1

- Ascer E, Bertolami MC, Venturinelli ML, Buccheri V, Souza J, Nicolau JC, Ramires JAO, Serrano CV (2004) Atorvastatin reduces proinflammatory markers in hypercholesterolemic patients. *Atherosclerosis* 177:161-166 doi:10.1016/j.atherosclerosis.2004.07.003
- Atalar E, Ozmen F, Haznedaroglu I, Açil T, Ozer N, Ovünç K, Aksöyek S, Kes S (2002) Effects of short-term atorvastatin treatment on global fibrinolytic capacity, and sL-selectin and sFas levels in hyperlipidemic patients with coronary artery disease. *Int J Cardiol* 84:227-231 doi:10.1016/s0167-5273(02)00148-1
- Azar RR, Kassab R, Zoghbi A, Aboujaoude S, El-Osta H, Ghorra P, Germanos M, Salame E (2006) Effects of clopidogrel on soluble CD40 ligand and on high-sensitivity C-reactive protein in patients with stable coronary artery disease. *Am Heart J* 151:521.e521-e524 doi:10.1016/j.ahj.2005.10.021
- Barale C, Frascaroli C, Senkeev R, Cavalot F, Russo I (2018) Simvastatin Effects on Inflammation and Platelet Activation Markers in Hypercholesterolemia. *Biomed Res Int* 2018:1-11 doi:10.1155/2018/6508709
- Chen Y, Xu F, Zhang Y, Ji Q, Sun Y, Lü R, Li R (2006) Effect of aspirin plus clopidogrel on inflammatory markers in patients with non-ST-segment elevation acute coronary syndrome. *Chin Med J (Engl)* 119:32-36
- Chu C, Lee K, Lee M, Su H, Voon W, Sheu S, Lai W (2006) Effects of atorvastatin and atorvastatin withdrawal on soluble CD40L and adipocytokines in patients with hypercholesterolaemia. *Acta Cardiol* 61:263-269 doi:10.2143/AC.61.3.2014826
- Cortellaro M, Cofrancesco E, Boschetti C, Cortellaro F, Mancini M, Mariani M, Paoletti RJT, Haemostasis (2000) Effects of fluvastatin and bezafibrate combination on plasma fibrinogen, t-plasminogen activator inhibitor and C reactive protein levels in coronary artery disease patients with mixed hyperlipidaemia (FACT study). *Thromb Haemost* 83:549-553
- Cottone S, A V, Vella M, Nardi E, Mulé G, Contorno A, Riccobene R, Cerasola G (1998) Changes of plasma endothelin and growth factor levels, and of left ventricular mass, after chronic AT1-receptor blockade in human hypertension. *Am J Hypertens* 11:548-553 doi:10.1016/s0895-7061(98)00027-2
- Derosa G, Mugellini A, Pesce RM, D'Angelo A, Maffioli P (2015) Perindopril and barnidipine alone or

- combined with simvastatin on hepatic steatosis and inflammatory parameters in hypertensive patients. *European journal of pharmacology* 766:31-36 doi:10.1016/j.ejphar.2015.09.030
- Derosa G, Mugellini A, Pesce RM, D'Angelo A, Maffioli P (2016) Barnidipine compared to lercanidipine in addition to losartan on endothelial damage and oxidative stress parameters in patients with hypertension and type 2 diabetes mellitus. *BMC Cardiovascular Disorders* 16:66-72 doi:10.1186/s12872-016-0237-z
- Dong Y, Yang D (2012) Efficacy of carvedilol and metoprolol for treatment of primary hypertension and their effects on vascular endothelial function. *Zhejiang Medical Journal* 34:904-906
- Doo YC, Kim DM, Oh DJ, Ryu KH, Rhim CY, Lee Y (2001) Effect of beta blockers on expression of interleukin-6 and C-reactive protein in patients with unstable angina pectoris. *Am J Cardiol* 88:422-424 doi:10.1016/s0002-9149(01)01693-9
- Fallois JV, Faulhaber HD (2001) Nebivolol, a beta blocker of the 3rd generation: modern therapy of arterial hypertension. Results of a multicenter observation study. *Praxis* 90:435-441
- Fogari R, Zoppi A, Lazzari P, Preti P, Mugellini A, Corradi L, Lusardi P (1998) ACE inhibition but not angiotensin II antagonism reduces plasma fibrinogen and insulin resistance in overweight hypertensive patients. *Journal of cardiovascular pharmacology* 32:616-620 doi:10.1097/00005344-199810000-00014
- Fujiwara T, Saito S, Osanai T, Kameda K, Abe N, Higuma T, Yokoyama J, Hanada H, Fukui K, Fukuda I, Okumura K (2008) Decreased plasma and cardiac matrix metalloproteinase activities in patients with coronary artery disease and treated with pravastatin. *European journal of pharmacology* 594:146-151 doi:10.1016/j.ejphar.2008.07.039
- Gómez-García A, Torres GM, Ortega-Pierres LE, Rodríguez-Ayala E, Alvarez-Aguilar C (2007) Rosuvastatin and metformin decrease inflammation and oxidative stress in patients with hypertension and dyslipidemia. *Rev Esp Cardiol* 60:1242-1249
- Glorioso N, Troffa C, Filigheddu F, Dettori F, Soro A, Parpaglia P, Collatina S, Pahor M (1999) Effect of the HMG-CoA reductase inhibitors on blood pressure in patients with essential hypertension and primary hypercholesterolemia. *Hypertension* 34:1281-1286 doi:10.1161/01.hyp.34.6.1281
- Heitzer T, Rudolph V, Schwedhelm E, Karstens M, Sydow K, Ortak M, Tschentscher P, Meinertz T, Boger R, Baldus S (2006) Clopidogrel improves systemic endothelial nitric oxide bioavailability in patients with coronary artery disease: evidence for antioxidant and

- antiinflammatory effects. *Arterioscler Thromb Vasc Biol* 26:1648-1652
doi:10.1161/01.ATV.0000225288.74170.dc
- Herrmann JM, Mayer EO (1988) A long-term study of the effects of celiprolol on blood pressure and lipid-associated risk factors. *American Heart Journal* 116:1416-1421 doi:10.1016/0002-8703(88)90133-0
- Hetzel S, DeMets D, Schneider R, Borzak S, Schneider W, Serebruany V, Schröder H, Hennekens CH (2013) Aspirin increases nitric oxide formation in chronic stable coronary disease. *Journal of cardiovascular pharmacology and therapeutics* 18:217-221 doi:10.1177/1074248413482753
- Hou L, Chi C, Yang Z, Wei L (2010) Correlated Study of Aspirin Resistance and P-selection in Platelet in Patients with Coronary Heart Disease. *Practical Journal of Cardiac Cerebral Pneumal and Vascular Disease* 18:740-741
- Hua Y, Xue J, Sun F, Zhu L, Xie M (2009) Aspirin inhibits MMP-2 and MMP-9 expressions and activities through upregulation of PPARalpha/gamma and TIMP gene expressions in ox-LDL-stimulated macrophages derived from human monocytes. *Pharmacology* 83:18-25 doi:10.1159/000166183
- Ikonomidis I, Andreotti F, Economou E, Stefanadis C, Toutouzas P, Nihoyannopoulos P (1999) Increased proinflammatory cytokines in patients with chronic stable angina and their reduction by aspirin. *Circulation* 100:793-798 doi:10.1161/01.cir.100.8.793
- Jiang S, Wang Y (2019) Clinical efficacy of atorvastatin calcium combined with nifedipine sustained-release tablets in the treatment of hypertension and its effect on TNF- α , CRP, IL-4 and IL-10. *Chinese Journal of Integrative Medicine on Cardio/Cerebrovascular Disease* 17:555-557
- Karalis DG, Ross AM, Vacari RM, Zarren H, Scott R (2002) Comparison of efficacy and safety of atorvastatin and simvastatin in patients with dyslipidemia with and without coronary heart disease. *The American Journal of Cardiology* 89:667-671
- Kinlav S, Rifai N, Libby P, Ganz P (2002) Effect of atorvastatin on C-reactive protein in patients with acute coronary syndromes: a substudy of the MIRACL trial. *Journal of the American College of Cardiology* 39:304 doi:10.1016/S0735-1097(02)81367-5
- Klinkhardt U, Bauersachs R, Adams J, Graff J, Lindhoff-Last E, Harder S (2003) Clopidogrel but not aspirin reduces P-selectin expression and formation of platelet-leukocyte aggregates in patients with atherosclerotic vascular disease. *Clin Pharmacol Ther* 73:232-241
doi:10.1067/mcp.2003.13

- Koh KK, Son JW, Ahn JY, Choi YM, Jin DK, Park GS, Choi IS, Sohn MS, Shin EK (2001) Non-lipid effects of statin on hypercholesterolemic patients established to have coronary artery disease who remained hypercholesterolemic while eating a step-II diet. *Coronary artery disease* 12:305-311 doi:10.1097/00019501-200106000-00006
- Koh KK, Son JW, Ahn JY, Jin DK, Kim HS, Choi YM, Kim DS, Jeong EM, Park GS, Choi IS, Shin EK (2002) Comparative effects of diet and statin on NO bioactivity and matrix metalloproteinases in hypercholesterolemic patients with coronary artery disease. *Arterioscler Thromb Vasc Biol* 22:e19-23 doi:10.1161/01.atv.0000030997.02059.bb
- Koh KK, Ahn JY, Jin DK, Han SH, Kim HS, Choi IS, Ahn TH, Shin EK, Jeong EM (2004) Comparative effects of statin and fibrate on nitric oxide bioactivity and matrix metalloproteinase in hyperlipidemia. *Int J Cardiol* 97:239-244 doi:10.1016/j.ijcard.2003.09.007
- Korish AA (2020) Clopidogrel Prophylaxis Abates Myocardial Ischemic Injury and Inhibits the Hyperlipidemia-Inflammation Loop in Hypercholesterolemic Mice. *Archives of Medical Research* 51:515-523 doi:10.1016/j.arcmed.2020.05.003
- Lacourcière Y, Poirier L, Lefebvre J, Provencher P, Arnott W (1992) Comparative effects of a new cardioselective beta-blocker nebivolol and nifedipine sustained-release on 24-hour ambulatory blood pressure and plasma lipoproteins. *Journal of Clinical Pharmacology* 32:660-666 doi:10.1002/j.1552-4604.1992.tb05778.x
- Li D, Feng Y, Zhang H, Bai Z (2003) Inhibition of early atherogenesis by ramipril and losartan in male rats with diet-induced hypercholesterolemia. *Journal of Clinical Cardiology (China)* 19:280-282
- Li J, Fang C, Wang C, Hui R (2005a) Effects of simvastatin on exercise-induced myocardial ischemia and plasma endothelin-1 concentrations in patients with stable angina. *Clin Chim Acta* 354:205-208 doi:10.1016/j.cccn.2004.10.012
- Li Z, Zhu S, Huang L, Tian Y, Yu L, Zhou Y, Wang J (2005b) Therapeutic effects of metoprolol on ventricular remodeling and proinflammatory cytokines in patients with chronic heart failure. *Chinese Heart Journal* 17:517-520
- Liu W, Shimada M, Xiao J, Hu D, Matsumori A (2009) Nifedipine inhibits the activation of inflammatory and immune reactions in viral myocarditis. *Life Sciences* 85:235-240
- Lopez Santi RG, Valeff EC, Duymovich CR, Mazziotta D, Mijailovsky NE, Filippa GC, Maltez R, Hernandez VA, Monroy AG, Borzi JG, Acheme RA, Etchegoyen MC,

- PROCORDISinvestigators (2005) Effects of an angiotensin-converting enzyme inhibitor (ramipril) on inflammatory markers in secondary prevention patients: RAICES Study. *Coron Artery Dis* 16:423-429 doi:10.1097/00019501-200510000-00002
- Makris TK, Stavroulakis GA, Krespi PG, Hatzizacharias AN, Triposkiadis FK, Tsoukala CG, Votteas VV, Kyriakidis MK (2000) Fibrinolytic/hemostatic variables in arterial hypertension: response to treatment with irbesartan or atenolol. *Am J Hypertens* 13:783-788 doi:10.1016/s0895-7061(00)00262-4
- Martinez MLL, Lopes LF, Coelho EB, Nobre F, Rocha JBT, Gerlach RF, Tanus-Santos JE (2006) Lercanidipine Reduces Matrix Metalloproteinase-9 Activity in Patients With Hypertension. *Journal of Cardiovascular Pharmacology* 47:117-122 doi:10.1097/01.fjc.0000196241.96759.71
- Nadar S, Blann AD, Lip GY (2006) Effects of aspirin on intra-platelet vascular endothelial growth factor, angiopoietin-1, and p-selectin levels in hypertensive patients. *Am J Hypertens* 19:970-978 doi:10.1016/j.amjhyper.2006.03.001
- Ohtsuka T, Hamada M, Hiasa G, Sasaki O, Suzuki M, Hara Y, Shigematsu Y, Hiwada K (2001) Effect of beta-blockers on circulating levels of inflammatory and anti-inflammatory cytokines in patients with dilated cardiomyopathy. *J Am Coll Cardiol* 37:412-417 doi:10.1016/s0735-1097(00)01121-9
- Onal IK, Altun B, Onal ED, Kirkpantur A, Oz SG, Turgan C (2009) Serum levels of MMP-9 and TIMP-1 in primary hypertension and effect of antihypertensive treatment. *Eur J Intern Med* 20:369-372 doi:10.1016/j.ejim.2008.10.003
- Qu H, Xiao Y, Jiang G, Wang Z, Zhang Y, Zhang M (2009) Effect of atorvastatin versus rosuvastatin on levels of serum lipids, inflammatory markers and adiponectin in patients with hypercholesterolemia. *Pharm Res* 26:958-964 doi:10.1007/s11095-008-9798-6
- Riesen WF, Engler H, Risch M, Korte W, Noseda G (2002) Short-term effects of atorvastatin on C-reactive protein. *European heart journal* 23:794-799 doi:10.1053/euhj.2001.2967
- Rizos E, Bairaktari E, Kostoula A, Hasiotis G, Achimastos A, Ganotakis E, Elisaf M, Mikhailidis DP (2003) The combination of nebivolol plus pravastatin is associated with a more beneficial metabolic profile compared to that of atenolol plus pravastatin in hypertensive patients with dyslipidemia: a pilot study. *Journal of cardiovascular pharmacology and therapeutics* 8:127-134 doi:10.1177/107424840300800206.

- Schieffer B, Bünte C, Witte J, Hoepfer K, Böger RH, Schwedhelm E, Drexler H (2004) Comparative effects of AT1-antagonism and angiotensin-converting enzyme inhibition on markers of inflammation and platelet aggregation in patients with coronary artery disease. *J Am Coll Cardiol* 44:362-368 doi:10.1016/j.jacc.2004.03.065
- Seljeflot I, Arnesen H, Andersen P, Aspelin T, Kierulf P (1999) Effects of doxazosin and atenolol on circulating endothelin-1 and von Willebrand factor in hypertensive middle-aged men. *J Cardiovasc Pharmacol* 34:584-588 doi:10.1097/00005344-199910000-00016
- Seljeflot I, Tonstad S, Hjermann I, Arnesen H (2002) Reduced expression of endothelial cell markers after 1 year treatment with simvastatin and atorvastatin in patients with coronary heart disease. *Atherosclerosis* 162:179-185 doi:10.1016/s0021-9150(01)00696-7
- Seljeflot I, Arnesen H, Pettersen A, Solheim S (2017) No difference in the effects of clopidogrel and aspirin on inflammatory markers in patients with coronary heart disease. *Thrombosis and Haemostasis* 96:660-664 doi:10.1160/th06-06-0337
- Su K (2017) Effect of combination of aspirin and atorvastatin on the concentration of serum sCD40L, MMP-2 in unstable angina pectoris patients. *Journal of Tropical Medicine* 17:226-229
- Tousoulis D, Andreou I, Tentolouris C, Antoniadis C, Papageorgiou N, Gounari P, Kotrogiannis I, Miliou A, Charakida M, Trikas A, Stefanadis C (2010) Comparative effects of rosuvastatin and allopurinol on circulating levels of matrix metalloproteinases and tissue inhibitors of metalloproteinases in patients with chronic heart failure. *Int J Cardiol* 145:438-443 doi:10.1016/j.ijcard.2009.05.051
- Tsutamoto T, Wada A, Maeda K, Mabuchi N, Hayashi M, Tsutsui T, Ohnishi M, Sawaki M, Fujii M, Matsumoto T, Kinoshita M (2000) Angiotensin II type 1 receptor antagonist decreases plasma levels of tumor necrosis factor alpha, interleukin-6 and soluble adhesion molecules in patients with chronic heart failure. *Journal of the American College of Cardiology* 35:714-721 doi:10.1016/s0735-1097(99)00594-x
- Vukovic PM, Maravic-Stojkovic VR, Peric MS, Jovic MD, Cirkovic MV, Gradinac SD, Djukanovic BP, Milojevic PS (2010) Steroids and statins: an old and a new anti-inflammatory strategy compared. *Perfusion* 26:31-37 doi:10.1177/0267659110385607
- Wang Y, Shi Y, Li S, Xu J, Li J (2017) Effects of Clopidogrel and Aspirin on the Serum Levels of hs-CRP, TNF- α and IL-6 in Patients with Coronary Heart Disease and Angina Pectoris. *Progress*

in *Modern Biomedicine* 17:327-330

Xiao Z, Theroux P (2004) Clopidogrel inhibits platelet-leukocyte interactions and thrombin receptor agonist peptide-induced platelet activation in patients with an acute coronary syndrome. *J Am Coll Cardiol* 43:1982-1988 doi:10.1016/j.jacc.2003.10.071

Xu E, Chen X (2013) The Effect of Clopidogrel on Serum Metalloproteinase-2, 3, 9 Levels in Patients with Unstable Angina and its Clinical Efficacy. *Journal of Radioimmunology* 26:801-803

Yin Y (2018) Effect of aspirin combined with clopidogrel on serum levels of hs-CRP, TNF- alpha and IL-6 in patients with coronary heart disease and angina pectoris. *Anatomy Research* 40:178-181

Zhai G, Zhu H, Qu B, Cai J (2005) Effect of low-dosage aspirin on vascular endothelial function of angina patients. *Journal of the Fourth Military Medical University* 26:2175-2177

Zhang X, Sun D, Wang W, Lin L (2013) The effect of clopidogrel on serum matrix metalloproteinase-9 and its inhibitor-1 in patients with ischemic stroke. *China Modern Doctor* 51:76-78

Zhang Y, Ding G (2013) Effect and curative observation of Clopidogrel on serum matrix metalloproteinase-3, 8 and 9 of cerebral ischemic stroke patients. *China Medical Herald* 10:76-78