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Review

Effects of Various Antihypertensive Drugs on Arterial Stiffness and Wave Reflections

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Key Words
Antihypertensive drugs · Arterial stiffness · Wave reflections · Randomized controlled trial

Abstract
We reviewed trials that tested the efficacy of antihypertensive drugs in reducing arterial stiffness and wave reflections as assessed by pulse wave velocity and augmentation index, respectively. Regardless of cross-over or parallel-group comparison design, placebo-controlled trials demonstrated that antihypertensive drugs were effective in reducing pulse wave velocity. In actively-controlled parallel-group comparison studies, this effect on arterial stiffness was more evident for angiotensin-converting enzyme inhibitors or angiotensin receptor blockers than other classes of antihypertensive drugs, particularly when brachial-ankle pulse wave velocity was measured. Regardless of cross-over or parallel-group comparison or placebo- or actively-controlled design, the reviewed trials showed that β-blockers were inferior to all the other classes of antihypertensive drugs in reducing augmentation index. However, these studies had a small sample size and a short follow-up time and did not link the changes in measurements of arterial function with cardiovascular events. Whether the superiority or inferiority is clinically relevant for cardiovascular protection and prevention remains to be investigated.

Introduction

In the past 2 decades, noninvasive measurements of arterial function are increasingly used as an intermediate measure of cardiovascular disease risk in therapeutic trials, such as antihypertensive therapy. Among various parameters of arterial function, pulse wave velocity and augmentation index measure arterial stiffness and wave reflections, respectively. Both

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measures can be accurately estimated within minutes with easy-to-use devices and may predict cardiovascular events above and beyond conventional cardiovascular risk factors, such as high blood pressure [1, 2]. However, at present, there is no specific treatment for increased arterial stiffness or wave reflections. Nonetheless, antihypertensive drugs, especially those of vasodilatating action, seem to be promising in this regard.

Since the early 1990s, several randomized controlled trials have been conducted to study the effects of various antihypertensive drugs on carotid-femoral or brachial-ankle pulse wave velocity and augmentation index. In the present review article, we summarized these trials to investigate whether and which antihypertensive drugs are efficacious in reducing arterial stiffness and wave reflections and to explore the clinical relevance of these arterial measurements for cardiovascular protection and prevention.

Arterial Effects of Antihypertensive Drugs in Placebo-Controlled Trials

Of the 27 placebo-controlled trials, 11 had a cross-over design (table 1) [3–13] and 16 had a parallel-group comparison design (table 2) [14–29]. Regardless of the design, these placebo-controlled studies had a sample size of tens and a follow-up time of weeks.

Of the 11 placebo-controlled cross-over trials, 6 and 5 had single [8–13] and multiple comparisons with placebo [3–7], respectively, and 2, 4, and 5 studied pulse wave velocity [11, 13], augmentation index alone [4, 5, 7, 10], and both [3, 6, 8, 9, 12], respectively (table 1). The results of these trials were generally consistent across various classes of antihypertensive drugs for pulse wave velocity but not augmentation index. Antihypertensive drugs were efficacious in reducing pulse wave velocity. However, most drugs had neutral effects on augmentation index, and β-blockers even had worse effects than placebo on this measure of wave reflections [6, 12].

Of the 16 placebo-controlled parallel-group comparison trials, 12 and 4 had single [15, 17–22, 24, 25, 27–29] and multiple comparisons with placebo [14, 16, 23, 26], respectively, and 8, 3, and 5 studied pulse wave velocity [14, 16, 19, 24–28], augmentation index alone [15, 18, 23], and both [17, 20–22, 29], respectively (table 2). The results of these parallel-group comparison trials were confirmatory for pulse wave velocity. Antihypertensive drugs significantly reduced pulse wave velocity in 10 of 18 drug comparisons from 13 trials. However, the results of these trials were slightly different for augmentation index. Antihypertensive drugs significantly reduced pulse wave velocity in 4 of 10 drug comparisons from 8 trials, none of which used β-blockers.

Arterial Effects of Antihypertensive Drugs in Actively-Controlled Trials

The actively-controlled trials also included those studies involving 2 or more drug comparisons with placebo. Of the 15 trials with a cross-over design (table 3) [1–5, 10, 30–38] and 31 trials with a parallel-group comparison design (table 4) [13, 16, 23, 26, 39–65], 6 [1–5, 10] and 4 [13, 16, 23, 26], respectively, were part of placebo-controlled studies. These actively-controlled studies also had a small sample size and short follow-up time with the exception of the CAFE (n = 2,073) [61], EXPLORE (n = 331) [50], and REASON trials (n = 406) [65]. These bigger studies investigated combination therapy and (except REASON [65]) had an open design, and hence had limited information on the comparison between drug classes.

Of the cross-over trials, 2, 7, and 6 studied pulse wave velocity [31, 37], augmentation index alone [2, 3, 5, 32, 33, 36, 38], and both [1, 4, 10, 30, 34, 35], respectively (table 3). These trials included 15 comparisons of angiotensin-converting enzyme (ACE) inhibitors with

Table 1. Randomized placebo-controlled double-blind cross-over studies

First author [Ref.]	Year	Subjects	Patients, n	Antihypertensive treatment(s)	Results	
					arterial stiffness	wave reflections
ACEIs						
Pannier [3]	2001	EH	20	perindopril	AUC cfPWV NS	AUC AIx perindopril better
Deary [4]	2002	EH	30	lisinopril	not measured	AIx NS
Morgan [5]	2004	EH	32	ACEIs	not measured	AIx NS
Hirata [6]	2005	CAD	30	ramipril	cfPWV ramipril better	AIx and AIx@HR75 ramipril better
Turner [7]	2006	intracranial aneurysms	19	perindopril	not measured	AIx NS
ARBs						
Asmar [8]	2002	EH/DM	20	telmisartan	cfPWV telmisartan better	AIx NS
Rajagopalan [9]	2006	healthy volunteers	33	valsartan	cfPWV NS	AIx NS
Turner [7]	2006	intracranial aneurysms	19	irbesartan	not measured	AIx NS
Kaufman [10]	2010	EH	10	losartan	not measured	AIx NS
β-Blockers						
Asmar [11]	1991	EH	14	bisoprolol	cfPWV bisoprolol better	not measured
Pannier [3]	2001	EH	20	atenolol	AUC cfPWV atenolol better	AUC AIx NS
Deary [4]	2002	EH	30	bisoprolol	not measured	AIx bisoprolol better
Morgan [5]	2004	EH	32	β-blockers	not measured	AIx NS
Hirata [6]	2005	CAD	30	atenolol	cfPWV atenolol better	AIx atenolol worse; AIx@HR75 NS
Dhakam [12]	2008	EH	16	nebivolol atenolol	aPWV nebivolol better aPWV atenolol better	AIx nebivolol worse AIx atenolol worse
CCBs						
Deary [4]	2002	EH	30	amlodipine	not measured	AIx NS
Morgan [5]	2004	EH	32	CCBs	not measured	AIx NS
Diuretics						
Deary [4]	2002	EH	30	bendrofluazide	not measured	AIx NS
Morgan [5]	2004	EH	32	diuretics	not measured	AIx NS
Davies [13]	2005	EH/DM	10	spironolactone	crPWV spironolactone better	not measured

ACEIs = ACE inhibitors; AIx = augmentation index; AIx@HR75 = AIx corrected for heart rate of 75 beats/min; aPWV = aortic pulse wave velocity; AUC = area under the curve; CAD = coronary artery disease; cfPWV = carotid-femoral pulse wave velocity; crPWV = carotid-radial pulse wave velocity; DM = diabetes mellitus; EH = essential hypertension; NS = not significantly different.

angiotensin receptor blockers (ARBs; n = 3) [5, 30, 31], β-blockers (n = 7) [1–4, 32–34], calcium channel blockers (CCBs; n = 3) [2, 3, 33], and diuretics (n = 2) [2, 3], 2 comparisons of ARBs with β-blockers [35, 36], 6 comparisons between 2 different β-blockers (n = 1) [10] or of β-blockers with CCBs (n = 3) [2, 3, 33] and diuretics (n = 2) [2, 3], 3 comparisons of CCBs with diuretics [2, 3, 37], and 2 comparisons of combination therapy with each of their component drugs [30, 38]. In these short-term cross-over studies, antihypertensive drugs had similar arterial effects, except that β-blockers were inferior to the other classes of antihypertensive drugs in reducing augmentation index in 11 of 14 comparisons with ACE inhibitors, ARBs, CCBs, or diuretics.

Of the parallel group trials, 20, 4, and 7 studied pulse wave velocity [13, 16, 26, 39–43, 46, 47, 49, 52–56, 58–60, 62], augmentation index alone [23, 48, 57, 63], and both [44, 45, 50, 51, 61, 64, 65], respectively (table 4). These trials included 20 comparisons of ACE inhibitors with ARBs (n = 6) [16, 39–43], β-blockers (n = 2) [13, 44], CCBs (n = 8) [13, 39, 40, 43–46], and diuretics (n = 4) [44, 47–49], 13 comparisons of ARBs with β-blockers (n = 2) [50, 51],

Table 2. Randomized placebo-controlled parallel-group comparison studies

First author [Ref.]	Year	Design	Subjects	Patients, n	Antihypertensive treatment(s)	Results	
						arterial stiffness	wave reflections
ACEIs							
Kahonen [14]	1998	DB	healthy volunteers	15	captopril	cfPWV captopril better	not measured
Dart [15]	2001	open	EH	111	perindopril	not measured	AIx NS
Ichihara [16]	2005	–	hemodialysis patients	42	trandolapril	baPWV trandolapril better	not measured
Yu [17]	2006	DB	hemodialysis patients	46	ramipril	cfPWV NS	AIx NS
Tsang [18]	2006	DB	IDD	21	quinapril	not measured	AIx NS
Ahimastos [19]	2007	DB	Marfan syndrome	17	perindopril	cfPWV and faPWV perindopril better	not measured
Rahman [20]	2007	DB	DM	21	ramipril	cfPWV NS	AIx NS
			IGT	19	ramipril	cfPWV NS	AIx ramipril better
Mitchell [21]	2007	open	CAD	300	trandolapril	cfPWV trandolapril better	AIx NS
Ahimastos [22]	2008	DB	PAD	40	ramipril	cfPWV ramipril better	AIx ramipril better
ARBs							
Klingbeil [23]	2002	DB	EH	40	valsartan	not measured	AIx valsartan better
Ichihara [16]	2005	–	hemodialysis patients	43	losartan	baPWV NS	not measured
Mitsuhashi [24]	2009	–	EH/hemodialysis patients	40	losartan	baPWV NS	not measured
β-Blockers							
Kahonen [14]	1998	DB	healthy volunteers	15	propranolol	cfPWV propranolol better	not measured
Kahonen [25]	2000	DB	healthy volunteers	31	bisoprolol, celiprolol, and propranolol	cfPWV bisoprolol and propranolol better; celiprolol worse	not measured
Ylitalo [26]	2005	DB	healthy volunteers	18	bisoprolol	cfPWV NS	not measured
CCBs							
London [27]	1990	DB	ESRD	37	nitrendipine	cfPWV nitrendipine better	not measured
Asmar [28]	1992	DB	EH	17	nitrendipine	cfPWV nitrendipine better	not measured
Kahonen [14]	1998	DB	healthy volunteers	15	verapamil	cfPWV NS	not measured
Ylitalo [26]	2005	DB	healthy volunteers	17	nisoldipine	cfPWV NS	not measured
Diuretics							
Klingbeil [23]	2002	DB	EH	40	hydrochlorothiazide	not measured	AIx NS
Edwards [29]	2009	DB	CKD	112	spironolactone	cfPWV spironolactone better	AIx spironolactone better

ACEIs = ACE inhibitors; AIx = augmentation index; baPWV = brachial-ankle pulse wave velocity; CAD = coronary artery disease; cfPWV = carotid-femoral pulse wave velocity; CKD = chronic kidney disease; DB = double-blinded; DM = diabetes mellitus; EH = essential hypertension; ESRD = end-stage renal dysfunction; faPWV = femoral-dorsalis pedis pulse wave velocity; IDD = isolated diastolic dysfunction; IGT = impaired glucose tolerance; NS = not significantly different; PAD = peripheral artery disease.

CCBs (n = 10) [39, 40, 43, 52–58], or a diuretic (n = 1) [23], 5 comparisons of β-blockers with CCBs (n = 4) [13, 26, 44, 59] or a diuretic (n = 1) [44], 7 comparisons between 2 different CCBs (n = 1) [40] or of CCBs with diuretics (n = 6) [44, 60–64], and 2 comparisons of combination therapy with one [65] or two of their component drugs [41]. In these studies, ACE inhibitors or ARBs tended to be more efficacious than other classes of antihypertensive drugs in reducing arterial stiffness, especially when brachial-ankle pulse wave velocity was measured in 11 trials [16, 40, 41, 43, 46, 52–54, 56, 58, 62]. The results were not consistent for other comparisons of pulse wave velocity or for studies on augmentation index, except that β-blockers were inferior to the other classes of antihypertensive drugs in reducing augmentation index in all 5 comparisons with an ACE inhibitor (n = 1) [44], ARBs (n = 2) [50, 51], a CCB (n = 1) [44], or a diuretic (n = 1) [44].

Table 3. Randomized actively-controlled cross-over studies

First author [Ref.]	Year	Design	Subjects	Patients, n	Comparison(s)	Results	
						arterial stiffness	wave reflections
ACEIs							
vs. ARBs							
Mahmud [30]	2002	SB	EH	12	captopril vs. valsartan	cfPWV NS	AIx NS
Turner [7]	2006	DB	intracranial aneurysms	19	perindopril vs. irbesartan	not measured	AIx NS
Ali [31]	2009	DB	EH	15	lisinopril vs. irbesartan	cfPWV NS	not measured
vs. β-blockers							
Chen [32]	1995	DB	EH	79	fosinopril vs. atenolol	not measured	AIx fosinopril better
Pannier [3]	2001	DB	EH	20	perindopril vs. atenolol	cfPWV atenolol better	AUC AIx peridopril better
Deary [4]	2002	DB	EH	30	lisinopril vs. bisoprolol	not measured	AIx lisinopril better
Morgan [5]	2004	DB	EH	32	ACEIs vs. β-blockers	not measured	AIx ACEIs better
Neal [33]	2004	DB	EH/liver transplantation	12	lisinopril vs. bisoprolol	not measured	AIx lisinopril better
Hirata [6]	2005	DB	CAD	30	ramipril vs. atenolol	cfPWV NS	AIx and AIx@HR75 ramipril better
Kaiser [34]	2006	DB	EH/DM	10	enalapril vs. nebivolol	cfPWV NS	AIx NS
vs. CCBs							
Deary [4]	2002	DB	EH	30	lisinopril vs. amlodipine	not measured	AIx NS
Morgan [5]	2004	DB	EH	32	ACEIs vs. CCBs	not measured	AIx NS
Neal [33]	2004	DB	EH/liver transplantation	12	lisinopril vs. amlodipine	not measured	AIx NS
vs. diuretics							
Deary [4]	2002	DB	EH	30	lisinopril vs. bendrofluazide	not measured	AIx NS
Morgan [5]	2004	DB	EH	32	ACEIs vs. diuretics	not measured	AIx NS
ARBs							
vs. β-blockers							
Dhakam [35]	2006	DB	EH	21	eprosartan vs. atenolol	cfPWV atenolol better	AIx eprosartan better
Izzo [36]	2012	SB	EH	30	lisinopril + valsartan vs. lisinopril + carvedilol	not measured	AIx NS
β-Blockers							
vs. β-blockers							
Dhakam [12]	2008	DB	EH	16	atenolol vs. nebivolol	aPWV NS	AIx nebivolol better
vs. CCBs							
Deary [4]	2002	DB	EH	30	bisoprolol vs. amlodipine	not measured	AIx amlodipine better
Morgan [5]	2004	DB	EH	32	β-blockers vs. CCBs	not measured	AIx CCBs better
Neal [33]	2004	DB	EH/liver transplantation	12	bisoprolol vs. amlodipine	not measured	AIx NS
vs. diuretics							
Deary [4]	2002	DB	EH	30	bisoprolol vs. bendrofluazide	not measured	AIx bendrofluazide better
Morgan [5]	2004	DB	EH	32	β-blockers vs. diuretics	not measured	AIx diuretics better

Table 3 (continued)

First author [Ref.]	Year	Design	Subjects	Patients, n	Comparison(s)	Results	
						arterial stiffness	wave reflections
CCBs *vs. diuretics*							
Asmar [37]	1993	DB	EH	16	felodipine vs. hydrochlorothiazide	cfPWV felodipine better	not measured
Deary [4]	2002	DB	EH	30	amlodipine vs. bendrofluazide	not measured	AIx NS
Morgan [5]	2004	DB	EH	32	CCBs vs. diuretics	not measured	AIx NS
Other							
Mahmud [30]	2002	SB	EH	12	captopril + valsartan vs. captopril vs. valsartan	cfPWV combination better	AIx combination better
Ferguson [38]	2008	DB	EH	22	fosinopril + hydrochlorothiazide vs. amlodipine vs. indapamide	not measured	AIx combination better

ACEIs = ACE inhibitors; AIx = augmentation index; AIx@HR75 = AIx corrected for heart rate of 75 beats/min; aPWV = aortic pulse wave velocity; AUC = area under the curve; CAD = coronary artery disease; cfPWV = carotid-femoral pulse wave velocity; DB = double-blinded; DM = diabetes mellitus; EH = essential hypertension; NS = not significantly different; SB = single-blinded.

Conclusions and Perspectives

Our narrative review was informative on three clinically relevant questions. First, antihypertensive drugs are effective in reducing arterial stiffness. However, this effect does not at all infer any benefit above and beyond blood pressure lowering. In contrast, because pulse wave velocity is dependent on systolic blood pressure, the therapeutic effect of antihypertensive drugs on arterial stiffness, to some extent if not entirely, can be attributable to their blood pressure lowering efficacy. Second, though all antihypertensive drugs reduce arterial stiffness, ACE inhibitors or ARBs might be more efficacious than other classes of antihypertensive drugs. This effect is more evident when brachial-ankle pulse wave velocity is measured. The mechanism remains to be elucidated. Third, as also evidenced by a recent meta-analysis of randomized controlled trials that compared β-blockers with the other classes of antihypertensive drugs [66], because of the intrinsic heart rate slowing effect, β-blockers are inferior to all the other classes of antihypertensive drugs in reducing augmentation index. However, whether this inferiority is clinically relevant for cardiovascular protection and prevention remains to be investigated.

In spite of a large number of trials that studied the efficacy of antihypertensive drugs in reducing pulse wave velocity and augmentation index, these studies had a small sample size and a short follow-up time and did not link the changes in measurements of arterial function with cardiovascular events. It is therefore imperative to combine the research force in the field of arterial functions to run adequately powered outcome trials to investigate whether arterial stiffness and wave reflections are clinically useful in monitoring the effect of antihypertensive treatment and other cardiovascular therapeutic approaches.

Table 4. Randomized actively-controlled parallel-group comparison studies

First author	Year	Design	Subjects	Patients, n	Comparison(s)	Results	
						arterial stiffness	wave reflections
ACEIs							
vs. ARBs							
Rajzer [39]	2003	open	EH	62	quinapril vs. losartan	cfPWV quinapril better	not measured
Takami [40]	2003	SB	EH	40	temocapril vs. valsartan	baPWV valsartan better	not measured
Ichihara [16]	2005	SB	hemodialysis patients	43	trandolapril vs. losartan	baPWV NS	not measured
Anan [41]	2005	SB	EH	21	perindopril vs. valsartan	baPWV NS	not measured
Rehman [42]	2007	DB	EH	39	perindopril vs. losartan	cfPWV NS	not measured
Li [43]	2009	SB	EH	68	perindopril vs. telmisartan	baPWV telmisartan better	not measured
vs. β-blockers							
Kahonen [14]	1998	DB	healthy volunteers	15	captopril vs. propranolol	aPWV NS	not measured
Mackenzie [44]	2009	DB	EH	32	perindopril vs. atenolol	cfPWV NS	AIx perindopril better
vs. CCBs							
London [45]	1994	SB	ESRD	24	perindopril vs. nitrendipine	cfPWV NS	AIx NS
Kahonen [14]	1998	DB	healthy volunteers	15	captopril vs. verapamil	aPWV NS	not measured
Rajzer [39]	2003	open	EH	75	quinapril vs. amlodipine	cfPWV quinapril better	not measured
Takami [40]	2003	–	EH	40	temocapril vs. cilnidipine	baPWV NS	not measured
				36	temocapril vs. nifedipine	baPWV temocapril better	not measured
Morimoto [46]	2008	–	EH	32	ARB + perindopril vs. ARB + amlodipine	baPWV NS	not measured
Mackenzie [44]	2009	DB	EH	29	perindopril vs. lercanidipine	cfPWV NS	AIx NS
Li [43]	2009	SB	EH	68	perindopril vs. amlodipine	baPWV amlodipine better	not measured
vs. diuretics							
Breithaupt-Grogler [47]	1996	DB	EH	17	cilazapril vs. hydrochlorothiazide	cfPWV NS	not measured
Jiang [48]	2005	DB	EH	101	enalapril vs. indapamide	not measured	AIx enalapril better
Mackenzie [44]	2009	DB	EH	28	perindopril vs. bendrofluazide	cfPWV NS	AIx NS
Kostka-Jeziorny [49]	2011	open	EH	66	perindopril vs. hydrochlorothiazide	cfPWV NS	not measured
ARBs							
vs. β-blockers							
Boutouyrie [50]	2010	open	EH	331	amlodipine + valsartan vs. amlodipine + atenolol	cfPWV NS	AIx and AIx@HR75 valsartan better
Vitale [51]	2012	DB	EH	65	irbesartan vs. nebivolol	cfPWV NS	AIx irbesartan better; AIx@HR75 NS
vs. CCBs							
Rajzer [39]	2003	open	EH	61	losartan vs. amlodipine	cfPWV NS	not measured
Takami [40]	2003	–	EH	40	valsartan vs. cilnidipine vs. nifedipine	baPWV valsartan better	not measured
Munakata [52]	2004	–	EH	41	valsartan vs. nifedipine	baPWV valsartan better	not measured
Ichihara [53]	2006	–	EH	100	valsartan vs. amlodipine	baPWV NS	not measured
Morimoto [54]	2006	–	EH	43	telmisartan vs. amlodipine	baPWV telmisartan better	not measured
Kosch [55]	2008	DB	EH	52	valsartan vs. metoprolol	cfPWV NS	not measured
Ishii [56]	2008	–	EH/DM	22	candesartan vs. CCBs	baPWV candesartan better	not measured
Schneider [57]	2008	DB	EH	156	irbesartan vs. atenolol	not measured	AIx irbesartan better
Li [43]	2009	SB	EH	68	telmisartan vs. amlodipine	baPWV telmisartan better	not measured
Tomiyama [58]	2011	–	EH	113	candesartan vs. amlodipine	baPWV candesartan better	not measured

Table 4 (continued)

First author	Year	Design	Subjects	Patients, n	Comparison(s)	Results	
						arterial stiffness	wave reflections
vs. diuretics							
Klingbeil [23]	2002	DB	EH	40	valsartan vs. hydrochlorothiazide	not measured	AIx valsartan better
β-Blockers							
vs. CCBs							
Merli [59]	1993	DB	EH	28	metoprolol vs. isradipine	cfPWV isradipine better	not measured
Kahonen [14]	1998	DB	healthy volunteers	15	propranolol vs. verapamil	cfPWV propranolol better	not measured
Ylitalo [26]	2005	DB	healthy volunteers	18	bisoprolol vs. nisoldipine	cfPWV NS	not measured
Mackenzie [44]	2009	DB	EH	31	atenolol vs. lercanidipine	cfPWV NS	AIx lercanidipine better
vs. diuretics							
Mackenzie [44]	2009	DB	EH	30	atenolol vs. bendrofluazide	cfPWV NS	AIx bendrofluazide better
CCBs							
vs. CCBs							
Takami [40]	2003	–	EH	36	cilnidipine vs. nifedipine	baPWV cilnidipine better	not measured
vs. diuretics							
White [60]	2003	DB	EH	139	amlodipine vs. eplerenone	cfPWV NS	not measured
Williams [61]	2006	open	EH	2,073	amlodipine vs. atenolol	cfPWV NS (n = 114)	AIx amlodipine better
Kaneshiro [62]	2009	DB	CKD	68	valsartan + amlodipine vs. valsartan + thiazide	baPWV NS	not measured
Mackenzie [44]	2009	DB	EH	27	lercanidipine vs. bendrofluazide	cfPWV NS	AIx NS
Doi [63]	2010	open	EH	37	azelnidipine vs. trichlormethiazide	not measured	AIx and AIx@HR75 azelnidipine better
Matsui [64]	2011	open	EH	207	azelnidipine vs. hydrochlorothiazide	cfPWV azelnidipine better	AIx NS
Other							
Asmar [65]	2001	DB	EH	406	perindopril + indapamide vs. atenolol	cfPWV NS	AIx combination better
Anan [41]	2005	–	EH	21	perindopril + valsartan vs. perindopril vs. valsartan	baPWV combination better	not measured

ACEIs = ACE inhibitors; AIx = augmentation index; AIx@HR75 = AIx corrected for heart rate of 75 beats/min; aPWV = aortic pulse wave velocity; baPWV = brachial-ankle pulse wave velocity; cfPWV = carotid-femoral pulse wave velocity; CKD = chronic kidney disease; DB = double-blinded; DM = diabetes mellitus; EH = essential hypertension; ESRD = end-stage renal dysfunction; NS = not significantly different; SB = single-blinded.

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