Table S1[1]. List of fitting parameters and boundaries of the search space used to generate virtual patients with arterial hypertension.

№	Parameters	Notations in the model	Ranges[2]	Units
01	Total metabolic intensity	A_1	0.00032 – 0.00128	mL^{-1}
02	Sympathetic sensitivity of the systemic microvessels	A_3	0.1 – 0.6	mL·mmHg^{-1}
03	Systemic arterial tone	A_9	0.07 – 0.09	mmHg·s·mL^{-1}
04	Normal level of vasopressin	C_{adh_norm}	1.0 – 13.3	pg·mL^{-1}
05	Normal level of aldosterone	C_{al_norm}	70 – 300	pg·mL^{-1}
06	Normal level of atriopeptin	C_{anp_norm}	7.4 – 152.0	ng·L^{-1}
07	Oxygen capacity of hemoglobin	C_H	1.32 – 1.39	mL·g^{-1}
08	Serum potassium	C_K	3.5 – 5.5	mEq·L^{-1}
09	Cardiac output (in the renal submodel)	CO	2.51 – 9.00	L·min^{-1}
10	Afferent arteriole diameter	d_{aa}	8.7 – 23.9	μm
11	Efferent arteriole diameter	d_{ea}	12.2 – 20.1	μm
12	Action threshold of the Frank-Starling law	$FS_{threshold0}$	0.0 – 40.0	mL
13	Basic systemic arterial elastance	G_{AL0}	0.33 – 1.67	mmHg·mL^{-1}
14	Basic pulmonary arterial elastance	G_{AR0}	0.08 – 0.26	mmHg·mL^{-1}
15	Left ventricular wall elasticity	G_{HL}	0.02 – 0.72	mmHg·mL^{-1}
16	Right ventricular wall elasticity	G_{HR}	0.02 – 0.72	mmHg·mL^{-1}
17	Basic elasticity of the systemic veins	G_{VL0}	0.01 – 0.05	mmHg·mL^{-1}
18	Basic elasticity of the pulmonary veins	G_{VR0}	0.01 – 0.05	mmHg·mL^{-1}
19	Plasma glucose	$glucose$	3.9 – 6.1	mmol·L^{-1}
20	Hematocrit	Hct	M: 40 – 54; W: 36 – 48	%
21	Hemoglobin	He	M: 140 – 180; W: 120 – 160	g·L^{-1}
22	Basic activity of the cardiac center	$Heart_{Base}$	0.01 – 1.00	–
23	The ratio of unstressed to stressed volume in the systemic arteries	k_{AL}	0.7 – 1.0	–
24	The ratio of unstressed to stressed volume in the pulmonary arteries	k_{AR}	0.7 – 1.0	–
25	The ratio of unstressed to stressed volume in the systemic veins	k_{VL}	0.7 – 1.0	–
26	The ratio of unstressed to stressed volume in the pulmonary veins	k_{VR}	0.7 – 1.0	–
27	The ratio of unstressed to stressed volume in the left ventricle	k_{HL}	0.0 – 0.3	–
28	The ratio of unstressed to stressed volume in the right ventricle	k_{HR}	0.0 – 0.3	–
29	Normal filtration coefficient	K_{FG_0}	0.0039 – 0.0162	L·min^{-1}·mmHg^{-1}
30	Inotropic status of the left ventricle	K_{L0}	0.5 – 0.8	–
31	Inotropic status of the right ventricle	K_{R0}	0.5 – 0.8	–
32	Afferent arteriole length	L_{aa}	101 – 123	μm
33	Efferent arteriole length	L_{ea}	124 – 152	μm
34	Initial value of the total exchangeable sodium	M_{sod}	2040 – 3950	mEq
35	Number of nephrons in the kidneys	$N_{nephrons}$	0.80*E*6 – 2.75*E*6	–

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[1] The substantiation of the parameter ranges can be found in the supplementary file to our basic study [Kutumova et al., 2021].

[2] **M** = men; **W** = women.

36	Normal fractional distal tubule sodium reabsorption	n_{ε_dt}	0.3 – 0.7	–
37	Normal fractional collecting duct sodium reabsorption	n_{η_cd}	0.6 – 1.0	–
38	Normal fractional proximal sodium reabsorption	n_{η_pt}	0.67 – 0.97	–
39	Hydrostatic pressure in the Bowman’s space	P_B	10.0 – 15.0	mmHg
40	Normal value of the glomerular hydrostatic pressure	P_{gh_norm}	48.0 – 63.0	mmHg
41	Initial value of the glomerular capillary oncotic pressure	P_{go}	23.6 – 34.0	mmHg
42	Renal venous pressure	P_v	2.0 – 6.0	mmHg
43	Normal plasma renin concentration	PRC_{nom}	3.42 – 69.4	pg·mL^{-1}
44	Nominal resistance of the interlobar, arcuate and interlobular arteries	$R_{preglom\_0}$	7.0 – 28.0	mmHg·min·l^{-1}
45	Renal venous resistance	R_v	11.3 – 20.1	mmHg·min·l^{-1}
46	Nominal body oxygen demand	RO_{20}	2.52 – 5.88	mL·s^{-1}
47	Arterial oxygen saturation	SpO_2	0.92 – 0.99	–
48	Total protein	TP	60.0 – 86.0	g·L^{-1}
49	Plasma urea concentration	$urea$	1.8 – 7.1	mmol·L^{-1}
50	Initial value of the total body water	TBW	$f(0.9 \cdot N_{BV}) – f(1.1 \cdot N_{BV})$[3]	L
51	Initial value of the venous oxygen content	VO_2	0.0855 – 0.1848	–
52	The equilibrium ratio of plasma renin activity to plasma renin concentration	X_{PRC_PRA}	0.61 – 1.42	fmol·min^{-1}·pg^{-1}
53	Basic conductivity of the systemic microvessels	Y_{ALVL0}	0.5 – 2.0	mL·s^{-1}·mmHg^{-1}
54	Basic conductivity of the pulmonary microvessels	Y_{ARVR0}	9.0 – 21.0	mL·s^{-1}·mmHg^{-1}
55	Nominal value of the macula densa sodium flow rate	$\Phi_{md\_sod\_0}$	1.0 – 4.0	mEq·min^{-1}
56	Sodium intake	Φ_{sodin}	0.0280 – 0.2088	mEq·min^{-1}
57	Normal value of the water intake	Φ_{win_norm}	0.00096 – 0.00312	L·min^{-1}

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[3] To calculate TBW, we used the formula $f(N_{BV}) = (N_{BV} – 650)/111.5$ [Moore, 1967], where N_{BV} is the estimate defined by the Nadler equation [Nadler et al., 1962]. We considered N_{BV} ± 10% as the range of total blood volume in normal humans.

Table S2[4]**.** List of constraints imposed on model variables in virtual hypertensive patients.

№	Variables	Notations/formulas in the model	Ranges[5]	Units
01	Arterial oxygen content	AO_2	0.145 – 0.244	–
02	Plasma angiotensin (1-7)	$ANG17$	12.7 – 34.9	fmol·mL^{-1}
03	Plasma angiotensin I	$ANGI$	2.5 – 15.0	fmol·mL^{-1}
04	Plasma angiotensin II	$ANGII$	3.3 – 7.1	fmol·mL^{-1}
05	Plasma vasopressin	C_{adh}	1.0 – 13.3	pg·mL^{-1}
06	Plasma aldosterone	C_{al}	70 – 300	pg·mL^{-1}
07	Plasma atriopeptin	C_{anp}	7.4 – 152.0	ng·L^{-1}
08	Plasma sodium	C_{sod}	137 – 147	mEq·L^{-1}
09	Cardiac output (in the heart submodel)	CO	2.51 – 9.00	L·min^{-1}
10	Ejection fraction	EF	50 – 80	%
11	Blood flow in the systemic microvessels	F_{ALVL}	> 0.0	mL·s^{-1}
12	Blood flow in the pulmonary microvessels	F_{ARVR}	> 0.0	mL·s^{-1}
13	Transaortic flow peak rate	F_{HLAL_p}	347.0 – 677.0	mL·s^{-1}
14	Transpulmonary flow peak rate	F_{HRAR_p}	264.5 – 793.0	mL·s^{-1}
15	Active peak filling rate (right ventricle)	F_{VLHR_ap}	M: 23 – 947; W: 54 – 680	mL·s^{-1}
16	Early peak filling rate (right ventricle)	F_{VLHR_ep}	M: 8 – 814; W: -17 – 701	mL·s^{-1}
17	The ratio of early to active peak filling rates (right ventricle)	F_{VLHR_ep}/F_{VLHR_ap}	M: -0.5 – 2.5; W: -0.4 – 2.5	–
18	Active peak filling rate (left ventricle)	F_{VRHL_ap}	M: 99 – 647; W: 58 – 508	mL·s^{-1}
19	Early peak filling rate (left ventricle)	F_{VRHL_ep}	M: 21 – 1034; W: -13 – 967	mL·s^{-1}
20	The ratio of early to active peak filling rates (left ventricle)	F_{VRHL_ep}/F_{VRHL_ap}	M: 0.3 – 5.9; W: 0.3 – 6.6	–
21	Systemic arterial elastance	G_{AL}	0.33 – 1.67	mmHg·mL^{-1}
22	Pulmonary arterial elastance	G_{AR}	0.08 – 0.26	mmHg·mL^{-1}
23	Glomerular filtration rate	GFR	0.060 – 0.135	L·min^{-1}
24	Total exchangeable sodium	M_{sod}	2040 – 3950	mEq
25	Normal fractional sodium reabsorption in the distal tubule and subsequent parts of the nephron	$n_{\varepsilon\ dt} + n_{\eta\_cd} - n_{\eta\_cd} \cdot n_{\varepsilon\ dt}$	0.78 – 0.98	–
26	Plasma osmolality	$osmolality$	275 – 295	mOsmol·kg^{-1}
27	Diastolic pulmonary arterial pressure	P_{AR_D}	4.0 – 12.0	mmHg
28	Systolic pulmonary arterial pressure	P_{AR_S}	15.0 – 30.0	mmHg
29	Glomerular hydrostatic pressure	P_{gh}	48.0 – 63.0	mmHg
30	Glomerular capillary oncotic pressure	P_{go}	23.6 – 34.0	mmHg
31	Left ventricular diastolic pressure	P_{HL_D}	1.0 – 18.0	mmHg
32	Left ventricular systolic pressure	P_{HL_S}	100 – 186	mmHg
33	Right ventricular diastolic pressure	P_{HR_D}	0.0 – 10.0	mmHg
34	Right ventricular systolic pressure	P_{HR_S}	15.0 – 30.0	mmHg

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[4] The substantiation of the ranges can be found in the supplementary file to our basic study [Kutumova et al., 2021].

[5] **M** = men; **W** = women.

35	Systemic venous pressure	P_{VL}	1.0 – 10.0	mmHg
36	Pulmonary venous pressure	P_{VR}	3.0 – 20.0	mmHg
37	Plasma renin activity	PRA	12.0 – 38.0	fmol·mL^{-1}·min^{-1}
38	Plasma renin concentration	PRC	3.42 – 69.4	pg·mL^{-1}
39	Resistance of the afferent vessels (arteries and arterioles)	R_{a_dyne}	3000 – 25000	dyn·s·cm^{-5}
40	Resistance of the efferent arterioles	R_{e_dyne}	1350 – 3400	dyn·s·cm^{-5}
41	Resistance of the interlobar, arcuate and interlobular arteries	$R_{preglom}$	7.0 – 28.0	mmHg·min·L^{-1}
42	Renal blood flow	RBF	0.623 – 1.730	L·min^{-1}
43	Renal vascular resistance	RVR	55.0 – 190.0	mmHg·min·L^{-1}
44	Total blood volume	V	$0.9 \cdot N_{BV} - 1.1 \cdot N_{BV}$[6]	mL
45	Left ventricular end-diastolic volume	V_{HL_KD}	M: 67 – 155; W: 56 – 104	mL
46	Left ventricular end-systolic volume	V_{HL_KS}	M: 22 – 58; W: 19 – 49	mL
47	Right ventricular end-diastolic volume	V_{HR_KD}	M: 124 – 256; W: 78 – 218	mL
48	Right ventricular end-systolic volume	V_{HR_KS}	M: 38 – 118; W: 20 – 92	mL
49	Venous oxygen content	VO_2	0.0855 – 0.1848	–
50	Systemic vascular resistance	$1/Y_{HLAL}+1/Y_{ALVL}+1/Y_{VLHR}$	0.5271 – 1.9608	s·mmHg·mL^{-1}
51	Pulmonary vascular resistance	$1/Y_{HRAR}+1/Y_{ARVR}+1/Y_{VRHL}$	0.0151 – 0.1353	s·mmHg·mL^{-1}
52	Fractional proximal sodium reabsorption	$\eta_{pt\_sodreab}$	0.67 – 0.97	–
53	Fractional sodium reabsorption in the distal tubule and subsequent parts of the nephron	$\eta_{dt\_sodreab} + \eta_{cd\_sodreab} - \eta_{dt\_sodreab} \cdot \eta_{cd\_sodreab}$	0.78 – 0.98	–
54	Water intake	Φ_{win}	0.00096 – 0.00312	L·min^{-1}

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[6] N_{BV} is an estimate defined by the Nadler equation [Nadler et al., 1962]. We considered $N_{BV} \pm 10\%$ as the range of total blood volume in normal humans.

Table S3. Baseline characteristics of patient populations in clinical trials of antihypertensive drugs[7]

References	Treatment scheme	Number of persons (M/F)	Age (years)	SBP/DBP (mmHg)	HR (beats/ min)	BMI (kg/m^2)	Population
Abate et al., 1998	HCTZ 12.5 mg 8 weeks	28 (13/15)	77.0 ± 5.9	170.7 ± 11.1/ 99.9 ± 3.2	79.4 ± 7.9	–	Mild or moderate hypertension (DBP: 96 – 115 mmHg). Exclusion criteria: hypersensitivity to the test drugs, renal or hepatic failure, severe hypertension, leukopenia, heart failure, angina pectoris, idiopathic hypercalciuria, recent stroke or myocardial infarction (within the past 3 months), uncontrolled diabetes, atrial fibrillation, or orthostatic hypotension.
Agabiti Rosei et al., 2005	Enalapril 20 mg 12 weeks	133 (73/60)	53 (22 – 78)	151 ± 11/ 96 ± 6	–	26 (19 – 30)	Mild to moderate essential hypertension (SBP: 140 – 179 mmHg, DBP: 90 – 109 mmHg). Exclusion criteria: grade 3 hypertension or orthostatic hypotension; history of cardiovascular or cerebrovascular ischaemic events in the last 6 months; history of intracerebral haemorrhage or subarachnoid haemorrhage in the last 6 months; clinically significant cardiac valvular disease; known hypersensitivity to enalapril or nifedipine or to ACE inhibitors or dihydropyridine calcium antagonist; uncorrected hypokalaemia or hyperkalaemia; second or third degree heart block in the absence of a cardiac pacemaker; evidence of clinically significant cardiac arrhythmia; BMI > 31 kg/m^2; unstable type 1 diabetes mellitus; concomitant treatment with potassium sparing diuretics; gastrointestinal disease resulting in malabsorption; liver disease; transaminase levels > 2.5 times the upper limit of normal; renal failure; serum creatinine > 2.0 mg/dl; any malignant disease that has required treatment within the last 5 years; dementia or psychosis; history of non-compliance, alcoholism or drug abuse; treatment with any other investigational drug in the 30 days prior to entering the study; any condition which in the opinion of the investigator could interfere with the study results or be considered detrimental to the patient's welfare; women of childbearing potential with no adequate contraception.
Brown et al., 2011	Aliskiren 150 mg 8 weeks	318 (164/154)	58.4 ± 10.8	161.2 ± 8.5/ 92.0 ± 10.6	–	29.5 ± 5.2	Essential hypertension (SBP: 150 – 180 mmHg, DBP < 110 mmHg). Possible concomitant diseases: diabetes. Exclusion Criteria: severe hypertension, pregnant or nursing (lactating) women, pre-menopausal women not taking accepted form of birth control, serum potassium ≥ 5.5 mEq/L, history of cardiovascular conditions, uncontrolled Type 1 or Type 2 diabetes mellitus, hypersensitivity to renin inhibitors, calcium channel blockers, or to drugs with similar chemical structures.
	Amlodipine 5 mg 8 weeks	316 (156/160)	58.1 ± 10.9	161.1 ± 8.2/ 93.0 ± 9.1	–	29.8 ± 5.7	
Corea et al., 1996	Amlodipine 5 mg 8 weeks	84 (48/36)	52.9 ± 8.9	161.8 ± 12.8/ 101.8 ± 4.5	73.3 ± 9.6	–	Mild to moderate essential hypertension (DBP: 95 – 120 mmHg). Exclusion criteria: overt heart failure; a history of heart failure or myocardial infarction in the preceding 3 months; second- or third-degree heart block; malignant hypertension; evidence of significant hepatic, renal, or gastrointestinal disease; pregnancy; and use of estrogen-progestogen preparations; intolerable adverse events, lack of therapeutic response (DBP > 120 mm Hg).
Cushman et al., 2012	HCTZ 12.5 mg 4 weeks	128 (66/62)	77.7 ± 4.8	164.6 ± 12.0/ 85.6 ± 9.1	71.2 ± 11.3	28.6 ± 4.9	Primary systolic hypertension (SBP: 150 – 200 mmHg). Possible concomitant diseases: diabetes. Exclusion criteria: recent use of investigational drugs, history of hypersensitivity to drugs in similar chemical classes, inability to discontinue prior antihypertensive medications, SBP ≥ 160 mmHg despite ≥ 3 antihypertensive drugs at screening, DBP ≥ 120 mmHg at any time during the screening or washout phases, known secondary hypertension, clinically significant cardiac arrhythmias or cardiac valvular disease, history or symptoms of chronic heart failure, orthostatic hypotension, uncontrolled diabetes, malignancies, significant autoimmune disorders, acute gout within the previous year, or renal, pancreatic, or hepatic impairment, recent history (< 6 months of screening) of stroke, transient ischemic attack, myocardial infarction, significant coronary artery disease, or atherosclerotic vascular disease.

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[7] **SBP** = systolic blood pressure; **DBP** = diastolic blood pressure; **HR** = heart rate; **BMI** = body mass index; **M** = male; **F** = female; **ACE** = angiotensin-converting enzyme; **ARB** = angiotensin-receptor blocker; **A150** = aliskiren 150 mg; **A300** = aliskiren 300 mg; **B5** = bisoprolol 5 mg, **L50** = losartan 50 mg; **n.s.** = not specified. The data are mean ± standard deviation or mean (range).

Derosa et al., 2014	Enalapril 20 mg 24 months	120 (58/62)	57.3 ± 6.1	155.6 ± 9.1/ 98.5 ± 7.2	–	26.1 ± 3.3	First diagnosis of essential hypertension (DBP: 90 – 110 mmHg, SBP: 140 – 180 mmHg), patients naive to antihypertensive treatment. Exclusion criteria: secondary hypertension, severe hypertension (SBP > 180 mmHg or DBP > 110 mmHg), hypertrophic cardiomyopathies due to aetiologies other than hypertension, history of heart failure or a left ventricular ejection fraction ≤ 50%, history of angina, stroke, transient ischaemic cerebral attack, coronary artery bypass surgery or myocardial infarction any time prior to visit 1, concurrent symptomatic arrhythmia, liver dysfunction (AST or ALT values exceeding 2-fold the upper limit), creatinine > 1.5 mg/dL and known hypersensitivity to the study drugs, pregnant women, women of childbearing potential, endocrine, infective or inflammatory disorders, patients taking anti-inflammatory medications.
Fagher et al., 1990	Enalapril 20 mg 4 weeks	22 (17/5)	37-59	163 ± 15/ 108 ± 7	75 ± 11	–	Newly discovered essential hypertension
Fermé et al., 1990	Enalapril 20 mg 4 weeks	31 (n.s.)	55 ± 2	172 ± 3/ 104 ± 1	77 ± 2	–	Mild to moderate arterial hypertension (DBP: 95 – 115 mmHg)
Gradman et al., 2005	Aliskiren 150 mg 8 weeks	127 (73/54)	55.0 ± 12.5	151.3 ± 11.1/ 98.8 ± 3.4	72.9 ± 9.4	30.7 ± 6.4	Mild-to-moderate essential hypertension (DBP: 95 – 110 mmHg). Exclusion criteria: severe hypertension (DBP ≥ 110 mmHg or SBP ≥ 180 mmHg), secondary hypertension, type 1 diabetes mellitus, type 2 diabetes mellitus with poor glucose control (HbA1c > 8% at screening), a history of cardiovascular disease (heart failure, myocardial infarction, unstable angina, transient ischemic cerebral attack), a history of malignancy or other life-threatening disease, any medical or surgical condition that might significantly alter the absorption, distribution, metabolism, or excretion of study drugs.
	Aliskiren 300 mg 8 weeks	130 (55/75)	56.0 ± 10.2	152.1 ± 10.2/ 98.8 ± 3.4	72.2 ± 8.2	30.5 ± 5.8	
Koh et al., 2004	Losartan 100 mg 2 months	47 (20/27)	57 ± 14	145 ± 14/ 89 ± 7	75 ± 14	25.2 ± 0.5	Hypercholesterolemic, hypertensive patients (LDL cholesterol levels ≥ 100 mg/dL, SBP ≥ 140 mmHg, DBP ≥ 90 mmHg). Exclusion criteria: severe hypertension, unstable angina, or acute myocardial infarction.
Kwakernaak et al., 2017	Aliskiren 300 mg 6 weeks	15 (15/0)	58 ± 12	149 ± 19/ 93 ± 12	–	30 ± 4	Essential hypertension (WHO criteria; either treated with antihypertensive medication or untreated ambulant SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg), weight excess (BMI: 27 – 35 kg/m^2), normal renal function (endogenous creatinine clearance ≥ 90 mL/min/1.73m^2), and normo- or microalbuminuria (urinary albuminuria excretion < 300 mg/day). Exclusion criteria: off-treatment SBP ≥ 180 mmHg and DBP ≥ 110 mmHg, history of cardiovascular disease (myocardial infarction, angina pectoris, percutanous transluminal coronary angioplasty, coronary artery bypass grafting, stroke, heart failure of stage I-IV of the New York Heart Association classification), diabetes mellitus, active malignancy, any medication and/or surgical or medical condition that might alter absorption, distribution, metabolism, or excretion of medication, history of hypersensitivity or contraindication to trial medication or radio-labeled tracers, history of angioedema, autonomic dysfunction, participation in any other clinical investigation within three months prior to start of the trial, blood or plasma donation within 3 months prior to initial dosing, and history of either drugs or alcohol abuse.
Lee et al., 2012	Losartan 50 mg 4 weeks	238 (167/71)	53.58 ± 9.61	149.17 ± 12.40/ 98.60 ± 5.68	–	–	Mild-to-moderate hypertension (DBP: 90 – 109 mmHg). Exclusion criteria: DBP < 90 mmHg or ≥ 110 mmHg; severe hypertension (SBP ≥ 200 mmHg); secondary hypertension; suspected severe systemic disease such as renal disease (serum creatinine ≥ 1.5 x upper limit of normal), gastrointestinal disorder, hematology disorder, or liver disease (aspartate transaminase and alanine transaminase ≥ 2 x upper limit of normal) that might affect the absorption, distribution, metabolism, and excretion of the study drugs; severe insulin-dependent diabetes or uncontrolled diabetes (glycated hemoglobin > 9%), patients whose usage or dose of an oral hypoglycemic agent was modified within the previous 12 weeks or patients who have experienced insulin administration; history of myocardial infarction or severe coronary arterial disease within the previous 6 months; clinically significant

							congestive heart failure or valvular heart disease; wasting disorder, autoimmune disease, or connective tissue disease; hepatitis B or C (including carrier); positive status for HIV; clinically significant abnormal laboratory test findings; patients under treatment with any medicine affecting blood pressure; patients with an allergic response or contraindication to angiotensin II antagonists; pregnant or breastfeeding women or women of child-bearing age not sterilized or who had no intention of using a contraceptive measure; alcoholic patients or patients with history/suspicion of drug abuse; participation in another clinical study within the previous 12 weeks from the screening visit.
Lithell et al., 1987	Bisoprolol 5 mg 4 weeks	97 (51/46)	51.8 ± 9.6	165.1 ± 17.4/ 103.2 ± 5.8	75.1 ± 9.6	26.3 ± 4.5	Mild to moderate hypertension (DBP: 95 – 120 mmHg). Possible concomitant diseases: history of coronary heart disease (3 patients), cerebrovascular disease (2), peripheral vascular disease (5), history of migraine (3), Raynaud's syndrome (5). Exclusion criteria: heart failure or sino-atrial block, atrio-ventricular block of any degree, left bundle branch block or bradycardia at rest (< 55 beats/min), patients who had experienced a myocardial infarction or a cerebrovascular accident during the last six months, patients with bronchial asthma, impaired renal function (serum creatinine > 150 μmol/L) or insulin-dependent diabetes mellitus, presence of other serious diseases.
Mallion, 2007	Enalapril 20 mg 4 weeks	156 (76/80)	53.3 ± 10.3	160.3 ± 9.7/ 100.8 ± 4.0	73.6 ± 9.4	27.7 ± 4.5	Mild to moderate hypertension (DBP: 95 – 115 mmHg). Exclusion criteria: severe or secondary forms of hypertension, two antihypertensive agents or more at the initial screening visit, cardiovascular or renal complications, insulin-dependent diabetes, concomitant medications judged to interfere with the study drugs.
Martina et al., 1999	Amlodipine 5 mg 6 weeks	14 (11/3)	51 ± 9	145 ± 10/ 100 ± 5	76 ± 9	30 ± 3	Untreated mild-to-moderate hypertension (DBP: 95 – 115 mmHg). Exclusion criteria: previous antihypertensive treatment.
	Losartan 50 mg 6 weeks	11 (5/6)	47 ± 6	154 ± 11/ 102 ± 4	79 ± 7	31 ±5	
Narkiewicz, 2007	Losartan 50 mg 4 weeks	162 (68/94)	57.9 ± 9.4	157.9 ± 12.0/ 99 ± 3	–	28.6 ± 3.1	Mild to moderate hypertension (DBP: 95 – 100 mmHg). Exclusion criteria: severe or secondary forms of hypertension, two antihypertensive agents or more at the initial screening visit, cardiovascular renal complication, insulin-dependent diabetes, concomitant medications known to interfere with the study drugs.
Nedogoda et al., 2013	Enalapril 20 mg 24 weeks	30 (15/15)	47.8 ± 8.1	157 ± 3/ 98 ± 3	79 ± 5	30.9 ± 2.2	Overweight or obese patients (BMI ≥ 27 kg/m^2) with hypertension (SBP: 140 –160 mmHg, DBP: 90 – 100 mmHg). Possible concomitant diseases: hypercholesterolaemia, microalbuminuria, left ventricular hypertrophy, history of coronary artery disease. Exclusion criteria: age < 18 years; hypersensitivity, intolerance or contraindications to ACE inhibitors or ARBs; unstable angina; heart failure; renal or hepatic insufficiency; grade 2 or 3 arterial hypertension (≥ 160/100 mmHg); a history of stroke; diagnosed or suspected secondary hypertension; or a serious illness affecting their prognosis.
	Losartan 100 mg 24 weeks	30 (15/15)	46.7 ± 8.2	157 ± 4/ 98 ± 3	76 ± 5	29.4 ± 3.6	
Oparil et al., 1996	Amlodipine 5 mg 4 weeks	93 (49/44)	54 ± 12	154.9 ± 16.7/ 101.0 ± 5.1	–	–	Mild-to-moderate hypertension (DBP: 95 – 114 mmHg), no known drug hypersensitivity to the study medications. Exclusion criteria: significant cardiovascular, cerebrovascular, renal, or hepatic disease; recent myocardial infarction; secondary hypertension; clinically significant laboratory abnormalities; pregnant women, and women of childbearing age who were not using an approved method of contraception.
	Losartan 50 mg 4 weeks	97 (53/44)	55 ± 13	153.7 ± 15.5/ 101.1 ± 5.3	–	–	
Oparil et al., 2008	Losartan 50 mg 4 weeks	127 (48/79)	50.1 ± 10.4	151.6 ± 8.2/ 99.1 ± 4.2	–	37.0 ± 6.1	Hypertension (SBP: 140 – 180 mmHg, DBP: 95 – 115 mmHg), without diabetes (fasting glucose < 126 mg/dL), taking no more than two antihypertensive agents, BMI > 30 kg/m^2, waist circumference > 40 (males)/> 35 (females) inches. Exclusion criteria: secondary hypertension, clinically significant renal disease (serum creatinine > 1.5 mg/dL or proteinuria > 2+ by urine dipstick) were excluded from the study.
	Losartan 100 mg 4 weeks						

Pareek et al., 2016	HCTZ 12.5 mg 12 weeks	18 (8/10)	47.72 ± 10.37	149.87 ± 4.50/ 93.39 ± 2.45	–	27.81 ± 5.08	Stage 1 essential hypertension (SBP: 140 – 159 mmHg, DBP: 90 – 99 mmHg). Exclusion criteria: (among others) secondary hypertension; diabetes; hyperuricemia; gout; chronic kidney disease; parathyroid diseases; recent cardiovascular disease or cardiovascular accident; abnormal renal function (serum creatinine: > 1.5 mg/dl; blood urea nitrogen > 20 mg/dl), abnormal liver function (aspartate aminotransferase, alanine aminotransferase, total bilirubin, or alkaline phosphatase > 2.5 x the upper limit of normal values); electrolyte imbalance; hypercalcemia; hypophosphatemia; women who were pregnant, lactating, or of childbearing potential and not practicing contraception; alcoholics; participation in a clinical trial within 30 days prior to enrollment.
Paterna et al., 2007	Bisoprolol 5 mg 6 months	87 (46/41)	49 ± 11	145.0 ± 15.5/ 88.9 ± 10.6	82.4 ± 14.2	–	Mild to moderate hypertension (DBP: 89 – 110 mmHg, SBP: 139 – 180 mmHg), absence of clinical findings suggestive of a secondary form of hypertension. Exclusion criteria: other cardiovascular disease (defined as myocardial infarction or angina pectoris, heart block, valvular disease, or heart failure and claudication), concomitant left ventricular hypertrophy defined according to echocardiography criteria or other target organ damage (including Keith-Wegener hypertensive retinopathy), proteinuria or renal disease, insulin-dependent or insulin-independent diabetes mellitus, electrolyte imbalance, alcoholism, psychiatric problems, or contraindications for β-blockers.
Pool et al., 2007	Aliskiren 150 mg 8 weeks	178 (101/77)	56.2 ± 12.4	154.1 ± 12.7/ 99.3 ± 3.7	72.3 ± 9.5	28.8 ± 4.2	Mild-to-moderate essential hypertension (DBP: ≥ 95 mmHg). Possible concomitant diseases (number of patients in A150/A300 groups): diabetes (15/13); history of coronary artery disease (2/1), myocardial infarction (0/1), transient ischemic attack (2/0). Exclusion criteria: severe hypertension (DBP ≥ 110 mmHg or SBP ≥ 180 mmHg), secondary hypertension, type 1 or uncontrolled (HbA1c > 8%) type 2 diabetes mellitus, history of severe cardiac or cerebrovascular disease, history of severe or life-threatening disease, and any medical or surgical condition that might alter the pharmacokinetics of study drugs, pregnant or lactating women.
	Aliskiren 300 mg 8 weeks	175 (100/75)	56.7 ± 11.9	152.9 ± 12.2/ 99.1 ± 3.4	72.7 ± 9.2	29.5 ± 5.1	
Porthan et al., 2009	Amlodipine 5 mg 4 weeks	183 (183/0)	51 ± 6	152 ± 13/ 100 ± 7	62 ± 7	26.5 ± 2.7	Prior antihypertensive drug treatment or DBP ≥ 95 mmHg, sinus rhythm. Exclusion criteria: treatment with three or more antihypertensive drugs, secondary hypertension, drug-treated diabetes mellitus, congestive heart failure, coronary heart disease, cerebrovascular disease, kidney disease (serum creatinine > 115 μmol/L), obstructive pulmonary disease, a disease treated with corticosteroids, clinically significant liver disease, abuse of drugs or alcohol, BMI ≥ 32 kg/m^2; the subject was withdrawn during the study, if the blood pressure level increased to 200/120 mm Hg; complete bundle branch block.
	Bisoprolol 5 mg 4 weeks						
	Losartan 50 mg 4 weeks						
Puig et al., 2007	Enalapril 20 mg 4 weeks	62 32/30	65.4 ± 4.6	168 ± 6/ 93 ± 9	–	28.3 ± 2.9	Hypertension (SBP: 160 – 179 mmHg, DBP < 110 mmHg, and mean daytime SBP ≥ 135 mmHg). Exclusion criteria: severe hypertension, a history of cardio- or cerebrovascular complications or diabetes mellitus requiring drug treatment.
Sun et al., 2016	Bisoprolol 5 mg 12 months	32 (15/17)	59.2 ± 9.9	147 ± 13/ 90 ± 7	74 ± 9	24.4 ± 3.4	Hypertension (SBP: 140 – 180 mmHg), renal failure (patients on hemodialysis for more than 6 months, who received erythropoietin dose adjusted to maintain hemoglobin between 110 and 120 g/L, and who achieved their dry weight assessed by bioimpedance method for at least 3 months). Possible additional antihypertensive medication: used on top of baseline (number of patients in B5/L50 groups): felodipine (11/9), terazosin (2/2). Exclusion criteria: clinical cardiovascular events within 6 months preceding entry into the study; diabetes mellitus (on the basis of past history and/or presence of overt fasting hyperglycemia of 7.0 mmol/L or greater); atrioventricular block and sinoatrial block, HR < 70 beats/min; chronic obstructive pulmonary disease; treatment with ACE inhibitors or angiotensin II receptor blockers during the past 6 months; age ≥ 75 years.
	Losartan 50 mg 12 months	33 (16/17)	57.1 ± 10.1	145 ± 11/ 92 ± 6	76 ± 10	23.1 ± 3.7	

Tham et al., 1993	Amlodipine 5 mg 4 weeks	14 (n.s.)	53 ± 10	156 ± 15/ 93 ± 7	77 ± 10	–	Essential hypertension (diastolic phase V blood pressure 95 – 110 mmHg).
Weber et al., 1995	Losartan 50 mg 4 weeks	21 (n.s.)	–	159.3 ± 16.6/ 101.0 ± 4.9	–	–	Hypertension (DBP: 95 – 115 mmHg, 24-hour average DBP ≥ 85 mmHg), patients within 30% of their ideal body weights. Exclusion criteria: secondary forms of hypertension; meaningful cardiopulmonary, renal, metabolic, or neurologic abnormalities; patients who required any form of concomitant cardiovascular medication or the long term use of any drugs that could affect blood pressure or other cardiovascular measurements.
	Losartan 100 mg 4 weeks	16 (n.s.)	–	150.9 ± 14.0/ 102.3 ± 4.7	–	–	
Wing et al., 2003	HCTZ 12.5 mg 6 weeks	17 (9/8)	61–81 (median 68)	163 ± 4/ 81 ± 8	69 ± 8	–	Isolated systolic hypertension (SBP: 160 – 210 mmHg, DBP < 95 mmHg). Exclusion criteria: secondary hypertension of any aetiology; a past history of malignant hypertension or blood pressure outside the inclusion limits; myocardial infarction, coronary angioplasty or coronary artery bypass grafting within the previous 6 months; a stroke or transient ischaemic attack within the past year; evidence of drug allergy or other contraindication to the administration of angiotensin receptor antagonists or diuretics; any evidence of cardiac failure, clinically significant cardiac valvular disease, cardiomyopathy or unstable angina; previously known moderate to severe left ventricular dysfunction; significant gastrointestinal disorders that could interfere with drug absorption; any clinically significant abnormalities in haematological or biochemical profiles; a history of gout or plasma urate concentration > 0.45 mmol/L; any other significant illness likely to interfere with survival (e.g. malignancy), or if it was anticipated that they would have poor compliance with study procedures.

Table S4. Response of human physiology to antihypertensive therapy[8]

Drugs	Patients	Treatment period	References	PRA	PRC	ANGI	ANGII	PAC	SSC	HR	CO	GFR	FF	RPF	RBF	RVR	ECFV	RA
Aliskiren, 300 mg	Weight excess, hypertension	6 weeks	Kwakernaak et al., 2017	↓	↑			NS	NS			NS	↓	↑		↓	NS	
Aliskiren, 150 to 300 mg	Hypertension, chronic kidney disease	24 weeks	Bokuda et al., 2018	↓	↑			↓				NS						
Aliskiren, 37.5, 75, 150, 300 mg	Essential hypertension	4 weeks	Stanton et al., 2003	↓						NS								
Aliskiren, 300 mg	Type 2 diabetes, hypertension, albuminuria	2 months	Persson et al., 2009	↓	↑	↓	↓	NS				↓						
Aliskiren, 300 mg	Hypertension, chronic kidney disease	6 weeks	Siddiqi et al., 2011						NS			NS						
Aliskiren, 75, 150, 300 mg	Mild-to-moderate essential hypertension	8 weeks	Villamil et al., 2007	↓	↑													
Aliskiren, 75, 150, 300, 600 mg	Healthy individuals	24 hours	Fisher et al., 2008	↓	↑	↓	↓					NS		↑				
Aliskiren, 150 to 300 mg	Elderly hypertensive individuals	6 months	Okada et al., 2017								NS							
Aliskiren, 150 mg	Advanced diabetic nephropathy	2 months	Ogawa et al., 2011									↑						
Aliskiren, 150 to 300 mg	Heart failure with reduced ejection fraction and decreased glomerular filtration rate	26 weeks	Schroten et al., 2015									↓	↓		NS			
Aliskiren, 300 mg	Uncomplicated type 1 diabetes mellitus	4 weeks	Cherney et al., 2012				↓	NS		NS		NS	NS	NS/↑	NS	NS		
Aliskiren, 150 mg (with 80 mg of valsartan *vs*. valsartan alone)	Hypertension with ischemic heart disease	24 weeks	Ozeki et al., 2014	↓				NS		↓								
Amlodipine, 10 mg	Mild to moderate hypertension	4 weeks	Licata et al., 1993	NS				NS				NS	NS	↑	↑	↓		
Amlodipine, 5 to 10 mg	Hypertensive renal transplant recipients	4 weeks	Toupance et al., 1994						NS									
Amlodipine, 5 mg	Renal transplant patients with normal renal function treated with cyclosporin	6 weeks	Iñigo et al., 2001	NS			↑					↑	↑	NS				↓
Amlodipine, 5 to 15 mg	Mild to moderate essential hypertension	12 weeks	Higashi et al., 1998	NS			NS	NS		NS		NS	↓	↑		↓		

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[8] **PRA** = plasma renin activity; **PRC** = plasma renin concentration; **ANGI** = plasma angiotensin I concentration; **ANGII** = plasma angiotensin II concentration; **PAC** = plasma aldosterone concentration; **SSC** = serum sodium concentration; **HR** = heart rate; **CO** = cardiac output; **GFR** = glomerular filtration rate; **FF** = filtration fraction; **RPF** = renal plasma flow; **RBF** = renal blood flow; **RVR** = renal vascular resistance; **ECFV** = extracellular fluid volume; **RA** = afferent arteriolar resistance; ↓ = decrease; ↑ = increase; **NS** = not significant.

Drugs	Patients	Treatment period	References	PRA	PRC	ANGI	ANGII	PAC	SSC	HR	CO	GFR	FF	RPF	RBF	RVR	ECFV	RA
Amlodipine, 5 to 10 mg	Essential hypertension	12 weeks	Tham et al., 1993							NS	NS							
Amlodipine, 5 to 10 mg	Mild to moderate essential hypertension	8 weeks	Delles et al., 2003									↑	↑	NS				↓
Amlodipine, 10 mg	Chronic kidney disease	8.5 hours	Morrone et al., 2003									↑	↓	↑		↓		
Amlodipine, 2.5 to 10 mg	Essential hypertension	6 weeks	Reams et al., 1987										NS		↑	↓	NS	
Amlodipine, 5 to 10 mg	Hypertensive patients with renal insufficiency following renal transplantation, who were maintained on a stable dose of cyclosporin A	8 weeks	Venkat-Raman et al., 1998									↑		↑				
Amlodipine, 5 mg	Cyclosporin A treated normotensive renal transplant patients with mild renal insufficiency	8 weeks	Venkat Raman et al., 1999									NS		↑				
Amlodipine, 10 mg	Mild to moderate essential hypertension	4 weeks	Ott et al., 2012									NS		NS				
Amlodipine, 5 mg	Non-diabetic patients with chronic renal failure	12 months	Satomura et al., 2009									NS	NS	NS	NS			NS
Bisoprolol, 2.5 to 5 mg	Hypertension	12 weeks	Eguchi et al., 2015						NS									
Bisoprolol, 10 mg	Normotensive and hypertensive subjects	1 week	Blumenfeld et al., 1999	↓			↓											
Bisoprolol, 10 mg	Essential hypertension	2 hours	Glück and Reubi, 1986	↓						↓		↓						
Bisoprolol, 5–10 mg	Drug-resistant hypertension	12 weeks	Williams et al., 2015						NS			↓						
Bisoprolol, 5 mg	Uncomplicated hypertension	1 year	Parrinello et al., 2009							↓	NS	NS	↓	NS	NS	NS		
Bisoprolol, 5 mg	Mild to moderate hypertension	6 months	Paterna et al., 2007							↓	NS	NS	NS	NS	NS	NS		
Bisoprolol, 10 mg	Essential hypertension	30 days	Honore, 1987							↓								
Bisoprolol, 10 mg	Sustained essential hypertension	4 weeks	Asmar et al., 1991							↓								
Bisoprolol, 10 mg	Uncomplicated essential hypertension	4 weeks	Leeman et al., 1993							↓	NS	NS			NS	↓		
Bisoprolol, 5 mg	Grade I to grade II essential hypertension	3 weeks	Suojanen et al., 2017							↓	NS							
Bisoprolol, 1.25 to 10 mg	Idiopathic pulmonary arterial hypertension	6 months	van Campen et al., 2016							↓	↓							

Drugs	Patients	Treatment period	References	PRA	PRC	ANGI	ANGII	PAC	SSC	HR	CO	GFR	FF	RPF	RBF	RVR	ECFV	RA
β-Blockers[9]	–	–	Mountokalakis, 1997; Bakris et al., 2006; Digne-Malcolm et al., 2016									↑/↓/ NS	NS/↓	↑/↓/ NS	↑/↓/ NS	↑/↓/ NS		
Enalapril, 20 mg	Normal subjects	4 hours	Nussberger et al., 1986	↑		↑	↓	↓										
Enalapril, 20 mg	Normal subjects	24 hours	Nussberger et al., 1992			↑	↓											
Enalapril, 20 mg	Healthy volunteers on a constant 100 mmol/d sodium diet	8 days	Nussberger et al., 2002[10]	↑	↑	↑	↓	↓										
Enalapril, 20 mg	Healthy normotensive subjects on a normal sodium diet	135 minutes	Schmitt et al., 1996	↑				NS				NS	NS	↑		↓		
Enalapril, 20 to 40 mg	Essential hypertension	8 weeks	Fagher et al., 1990	↑			↓	↓	NS									
Enalapril, 10 mg	Hypertension, chronic renal failure	6 weeks	Klein et al., 2003	↑													NS	
Enalapril, 20 mg (and concomitant medical therapy)	Moderate or severe chronic heart failure	8 weeks	Dickstein et al., 1995						NS									
Enalapril, 5 mg	Salt-resistant normotensive individuals	24 hours	Natarajan et al., 2016							NS			NS					
Enalapril, 2.5 to 20 mg	Long-term progression of left ventricular dilatation, asymptomatic systolic dysfunction	1 year, 13 – 45 months	Konstam et al., 1993							NS	NS							
Enalapril, 5 mg	Chronic heart failure	4 weeks	Kamishirado et al., 1997							NS								
Enalapril, 20 mg	Essential hypertension	4 weeks	Ajayi et al., 1989							↓								
Enalapril, 20 mg	Chronic kidney disease	4 hours	Morrone et al., 2003									↓	↓	↑		↓		
Enalapril, 10 to 40 mg	Essential hypertension	1, 6 weeks	Semplicini et al., 1986									NS	NS	NS			↑/NS	
Enalapril, 10 to 40 mg	Mild, uncomplicated hypertension	12 weeks	Simon et al., 1983[11]	↑								↑		↑				

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[9] Some members of the β-blocker class increase GFR and RBF [Mountokalakis, 1997; Bakris et al., 2006; Digne-Malcolm et al., 2016]. Therefore, we considered an increase in these variables as a possible long-term effect of bisoprolol.

[10] This example is also described in [Wiggins and Kelly, 2009].

[11] This example is also described in [Digne-Malcolm et al., 2016].

Drugs	**Patients**	**Treatment period**	**References**	**PRA**	**PRC**	**ANGI**	**ANGII**	**PAC**	**SSC**	**HR**	**CO**	**GFR**	**FF**	**RPF**	**RBF**	**RVR**	**ECFV**	**RA**
Enalapril, 20 to 40 mg	Essential hypertension	8 weeks	Bauer, 1984 Bauer and Jones, 1984[11]									NS/↑	NS/↓	NS/↑	NS/↑	↓		
HCTZ, 6.25, 12.5, 25 mg	Mild-to-moderate essential hypertension	8 weeks	Villamil et al., 2007	↑	↑ (25 mg)													
HCTZ, 25 to 100 mg	Essential hypertension	3 months	Lijnen et al., 1981	↑		↑	↑	↑										
HCTZ, 25 mg	Mild to moderate hypertension without cardiac or renal disease	8 weeks	Scaglione et al., 1992						NS	NS		NS	NS	NS	NS	↓		
HCTZ, 25 mg	Mild to moderate hypertension without cardiac or renal disease	4 weeks	Scaglione et al., 1995						NS	NS		NS	NS	NS	NS	↓		
HCTZ, 25 mg	Healthy individuals	28 days	Devineni et al., 2014						NS									
HCTZ, 12.5 to 50 mg	Essential hypertension with or without left ventricular hypertrophy	6 months	Roman et al., 1998	↑			NS		NS									
HCTZ, 100 mg	Essential hypertension	9 months	van Brummelen et al., 1979		↑							NS	NS/↓		↑/ NS	↓		
HCTZ, 100 mg	Essential hypertension	1, 4, 12, 24, 36 weeks	van Brummelen et al., 1980		↑					↑/NS vs ↓[12]	NS/ ↓/↑							
HCTZ	Stage 1 or 2 hypertension	up to 2 year	Materson et al., 1998							NS/ ↓/↑								
HCTZ, 50 mg	Essential hypertension	4 weeks	Ajayi et al., 1989							↑								
HCTZ, 50 mg	Chronic kidney disease stages 1–3 and a urinary albumin-to-creatinine ratio over 300 mg/g	4 weeks	Morales et al., 2015		↑			NS	NS			↓						
HCTZ, 50 to 100 mg (mean, 86 mg)	Essential hypertension	6 months	Leth, 1970														↓/NS	
HCTZ, 25 mg	Severe renal failure, hypertension	1 month	Dussol et al., 2005									↓	NS	↓				
HCTZ, 25 mg	Hypertension and stage 4 or 5 chronic kidney disease	3 months	Dussol et al., 2012									NS	↓	NS		NS		
Thiazide diuretics	–	–	Mountokalakis, 1997									↑/ NS	NS		↑/ NS	↓		
Losartan, 100 mg	Healthy volunteers	7 days	Goldberg et al., 1993	↑			↑	NS										

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[12] Responders *vs* non-responders

Drugs	Patients	Treatment period	References	PRA	PRC	ANGI	ANGII	PAC	SSC	HR	CO	GFR	FF	RPF	RBF	RVR	ECFV	RA
Losartan, 50 mg	Healthy normotensive subjects on a normal sodium diet	135 minutes	Schmitt et al., 1996	NS				↓				NS	NS	↑		↓		
Losartan, 100 mg	Essential hypertension	4 weeks	Stanton et al., 2003	↑						NS								
Losartan, 50 mg	Hypertensive subjects with type 2 diabetes and albumin excretion rates of 10–200 µg/min	4 weeks	Houlihan et al., 2002	↑			↑	↑/NS				NS	NS	NS				
Losartan, 100 mg	Hypertension, chronic renal failure	6 weeks	Klein et al., 2003	↑													NS	
Losartan, 5, 10, 25, 75, 150 mg	Congestive heart failure	24 hours	Gottlieb et al., 1993	↑			↑	↓										
Losartan, 25, 50 mg (and concomitant medical therapy)	Moderate or severe chronic heart failure	8 weeks	Dickstein et al., 1995						NS									
Losartan, 50 mg	Hypertension, IgA nephropathy	12 months	Ohashi et al., 2002	↑					NS			NS	NS	NS				
Losartan, 50 mg	Insulin-dependent diabetes mellitus, microalbuminuria	3, 7, 28 days	Buter et al., 2001	↑/ NS			↑/ NS	↓/ NS	NS			NS	↓	↑				
Losartan, 6.25 to 50 mg	Portal hypertensive patients with cirrhosis treated endoscopically after a variceal bleeding episode	6 weeks	González-Abraldes et al., 2001				↑	↓		NS	NS	NS/↓						
Losartan, 25 to 50 mg	Renal transplant patients with normal renal function treated with cyclosporin	6 weeks	Iñigo et al., 2001	↑			↑					NS	↓	NS				↓
Losartan, 50 to 100 mg (with possible HCTZ 12.5 mg once daily for the last 3 weeks)	Mild to moderate essential hypertension	9 weeks	Dobovisek et al., 2005							↓								
Losartan, 50 mg	Uncomplicated hypertension	1 year	Parrinello et al., 2009							NS	NS	NS	↓	NS	NS	NS		
Losartan, 50 mg	Hypertension without renal or cardiovascular disease	6 months, 1 year	Paterna et al., 2000									NS	↓	NS	NS	↓/NS		
Losartan, 12.5 to 50 mg	Essential hypertension	3 years	De Rosa et al., 2002									↑						

Table S5. Simulated effect of aliskiren 150 mg (A150), aliskiren 300 mg (A300), amlodipine 5 mg (A5), bisoprolol 5 mg (B5), enalapril 20 mg (E20), HCTZ 12.5 mg (H12.5), losartan 100 mg (L100), and losartan 50 mg (L50) on model variables in the virtual population of hypertensive patients (n = 186) during 4 weeks of treatment, mean ± SD.

Parameters	Baseline	A150	A300	E20	L50	L100	A5	B5	H12.5
Total body water	37.3 ± 4.3	37.3 ± 4.3	37.2 ± 4.3	37.1 ± 4.3	37.3 ± 4.3	37.2 ± 4.3	37.1 ± 4.3	37.9 ± 4.3	36.9 ± 4.3
Systolic blood pressure	154 ± 7	146 ± 7	143 ± 7	139 ± 8	146 ± 7	141 ± 8	144 ± 7	147 ± 8	141 ± 9
Diastolic blood pressure	101 ± 6	93 ± 6	91 ± 5	89 ± 5	93 ± 6	90 ± 5	93 ± 5	88 ± 6	92 ± 5
Heart rate	76 ± 7	74 ± 8	75 ± 8	77 ± 8	74 ± 8	76 ± 8	80 ± 7	66 ± 7	80 ± 10
Systemic vascular resistance	0.89 ± 0.09	0.88 ± 0.09	0.88 ± 0.09	0.87 ± 0.09	0.88 ± 0.09	0.87 ± 0.09	0.91 ± 0.10	0.86 ± 0.09	0.89 ± 0.09
Systolic pulmonary arterial pressure	17.4 ± 1.3	17.3 ± 1.4	17.1 ± 1.4	16.7 ± 1.4	17.3 ± 1.4	16.9 ± 1.4	17.4 ± 1.4	18.4 ± 1.6	16.6 ± 1.6
Diastolic pulmonary arterial pressure	11.2 ± 0.7	11.1 ± 0.7	11.0 ± 0.7	10.8 ± 0.7	11.1 ± 0.7	10.9 ± 0.7	11.3 ± 0.7	11.6 ± 0.9	10.8 ± 0.8
Pulmonary vascular resistance	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.101 ± 0.013	0.099 ± 0.013	0.100 ± 0.013
Stroke volume	70 ± 7	70 ± 7	69 ± 7	66 ± 8	70 ± 7	68 ± 7	67 ± 6	79 ± 9	64 ± 9
Ejection fraction	64 ± 7	64 ± 7	64 ± 7	63 ± 7	64 ± 7	63 ± 7	64 ± 7	67 ± 7	62 ± 7
Cardiac output	5.3 ± 0.5	5.2 ± 0.5	5.1 ± 0.5	5.1 ± 0.5	5.2 ± 0.5	5.1 ± 0.5	5.4 ± 0.5	5.2 ± 0.5	5.1 ± 0.5
LV peak systolic pressure	172.4 ± 7.0	163.4 ± 7.4	160.5 ± 7.5	156.3 ± 7.9	163.6 ± 7.4	158.9 ± 7.6	163.3 ± 6.9	165.2 ± 8.3	158.6 ± 8.9
LV end-diastolic pressure	8.0 ± 1.1	8.1 ± 1.1	8.0 ± 1.1	7.7 ± 1.1	8.1 ± 1.1	7.9 ± 1.1	7.8 ± 1.1	8.9 ± 1.3	7.5 ± 1.2
LV end-systolic volume	40 ± 11	40 ± 11	40 ± 11	40 ± 11	40 ± 11	40 ± 11	40 ± 10	41 ± 12	40 ± 11
LV end-diastolic volume	110 ± 13	111 ± 14	109 ± 14	106 ± 14	111 ± 14	108 ± 14	107 ± 13	120 ± 15	104 ± 15
RV peak systolic pressure	19.6 ± 1.4	19.5 ± 1.4	19.2 ± 1.4	18.9 ± 1.4	19.5 ± 1.4	19.1 ± 1.4	19.7 ± 1.4	20.6 ± 1.6	18.8 ± 1.7
RV end-diastolic pressure	5.9 ± 1.1	6.0 ± 1.1	5.9 ± 1.1	5.7 ± 1.1	6.0 ± 1.1	5.8 ± 1.1	5.7 ± 1.1	6.6 ± 1.2	5.5 ± 1.1
RV end-systolic volume	47 ± 12	48 ± 12	48 ± 12	47 ± 12	48 ± 12	47 ± 12	46 ± 11	51 ± 15	46 ± 11
RV end-diastolic volume	117 ± 14	118 ± 14	116 ± 14	113 ± 14	118 ± 14	115 ± 14	114 ± 14	130 ± 18	111 ± 16
Aortic valve peak flow	564 ± 65	561 ± 67	551 ± 67	535 ± 66	561 ± 67	545 ± 66	555 ± 63	610 ± 81	529 ± 74
Pulmonary valve peak flow	542 ± 75	539 ± 77	530 ± 76	516 ± 76	540 ± 77	525 ± 76	538 ± 74	582 ± 87	512 ± 83
LV early peak filling rate	628 ± 124	641 ± 127	627 ± 124	605 ± 120	641 ± 127	619 ± 123	630 ± 121	737 ± 157	590 ± 131
LV active peak filling rate	418 ± 42	389 ± 42	378 ± 42	361 ± 42	389 ± 42	371 ± 42	376 ± 37	402 ± 47	365 ± 43
RV early peak filling rate	571 ± 100	586 ± 103	577 ± 101	562 ± 98	587 ± 103	572 ± 100	585 ± 99	661 ± 123	549 ± 107
RV active peak filling rate	529 ± 55	493 ± 54	480 ± 53	461 ± 53	493 ± 54	473 ± 53	475 ± 49	505 ± 58	466 ± 55
Glomerular filtration rate	0.097 ± 0.018	0.097 ± 0.018	0.097 ± 0.018	0.097 ± 0.018	0.097 ± 0.018	0.097 ± 0.018	0.105 ± 0.016	0.097 ± 0.018	0.091 ± 0.022
Renal blood flow	1.10 ± 0.15	1.19 ± 0.16	1.19 ± 0.16	1.20 ± 0.16	1.19 ± 0.16	1.20 ± 0.16	1.20 ± 0.16	1.19 ± 0.16	1.24 ± 0.17
Filtration fraction	0.16 ± 0.04	0.15 ± 0.04	0.15 ± 0.04	0.15 ± 0.04	0.15 ± 0.04	0.15 ± 0.04	0.16 ± 0.04	0.15 ± 0.04	0.13 ± 0.04
Filtration coefficient	0.010 ± 0.003	0.013 ± 0.004	0.014 ± 0.004	0.017 ± 0.005	0.013 ± 0.004	0.015 ± 0.005	0.010 ± 0.003	0.014 ± 0.004	0.009 ± 0.003
Renal vascular resistance	105.8 ± 14.2	91.0 ± 12.7	88.7 ± 12.5	86.0 ± 12.3	91.1 ± 12.7	87.6 ± 12.4	89.7 ± 11.9	88.4 ± 12.5	85.0 ± 11.2
Afferent arteriolar resistance	4842 ± 825	4093 ± 747	3980 ± 739	3852 ± 734	4098 ± 747	3928 ± 737	3795 ± 679	3966 ± 738	3628 ± 635
Efferent arteriolar resistance	2606 ± 458	2117 ± 377	2037 ± 364	1942 ± 348	2121 ± 378	1999 ± 357	2342 ± 411	2029 ± 362	2084 ± 365
Macula densa sodium flow rate	2.0 ± 0.8	1.9 ± 0.8	1.9 ± 0.8	1.9 ± 0.8	1.9 ± 0.8	1.9 ± 0.8	2.0 ± 0.8	1.9 ± 0.8	1.3 ± 0.5
Fractional proximal sodium reabsorption	0.86 ± 0.06	0.86 ± 0.06	0.86 ± 0.06	0.86 ± 0.06	0.86 ± 0.06	0.86 ± 0.06	0.87 ± 0.06	0.86 ± 0.06	0.89 ± 0.06
Fractional distal sodium reabsorption	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.92 ± 0.04
Sodium	143.5 ± 1.3	143.5 ± 1.3	143.4 ± 1.3	143.4 ± 1.3	143.5 ± 1.3	143.4 ± 1.3	143.5 ± 1.3	143.4 ± 1.3	142.6 ± 1.3
Plasma renin activity	31.8 ± 3.6	12.7 ± 1.4	9.9 ± 1.1	217.7 ± 24.9	99.2 ± 11.3	163.3 ± 18.6	32.5 ± 3.7	9.6 ± 1.1	47.2 ± 5.3
Plasma renin concentration	33.1 ± 8.1	104.6 ± 25.6	143.3 ± 35.1	226.7 ± 55.5	103.3 ± 25.3	170.1 ± 41.7	33.8 ± 8.3	10.0 ± 2.4	49.1 ± 11.9
Plasma angiotensin I concentration	8.6 ± 1.0	3.4 ± 0.4	2.7 ± 0.3	77.4 ± 8.8	26.7 ± 3.0	44.0 ± 5.0	8.8 ± 1.0	2.6 ± 0.3	12.7 ± 1.4
Plasma angiotensin II concentration	5.4 ± 0.6	2.2 ± 0.2	1.7 ± 0.2	1.2 ± 0.1	19.1 ± 2.2	31.7 ± 3.6	5.5 ± 0.6	1.6 ± 0.2	8.0 ± 0.9
Plasma aldosterone concentration	182.4 ± 56.5	130.8 ± 40.5	119.5 ± 37.0	105.4 ± 32.7	131.3 ± 40.7	113.9 ± 35.3	183.7 ± 57.0	118.2 ± 36.7	190.4 ± 58.6

Table S6. Simulated effect of aliskiren 150 mg (A150), aliskiren 300 mg (A300), and their dual combinations with amlodipine 5 mg (A5), bisoprolol 5 mg (B5), and HCTZ 12.5 mg (H12.5) on model variables in the virtual population of hypertensive patients (n = 186) during 4 weeks of treatment, mean ± SD.

Parameters	Baseline	A150	A150/A5	A150/B5	A150/H12.5	A300	A300/A5	A300/B5	A300/H12.5
Total body water	37.3 ± 4.3	37.3 ± 4.3	37.0 ± 4.3	37.4 ± 4.3	36.8 ± 4.3	37.2 ± 4.3	36.8 ± 4.3	37.3 ± 4.3	36.6 ± 4.3
Systolic blood pressure	154 ± 7	146 ± 7	135 ± 7	137 ± 9	131 ± 9	143 ± 7	131 ± 7	134 ± 10	127 ± 9
Diastolic blood pressure	101 ± 6	93 ± 6	85 ± 5	83 ± 6	84 ± 5	91 ± 5	83 ± 5	82 ± 6	82 ± 5
Heart rate	76 ± 7	74 ± 8	80 ± 8	72 ± 8	81 ± 11	75 ± 8	82 ± 8	73 ± 9	83 ± 12
Systemic vascular resistance	0.89 ± 0.09	0.88 ± 0.09	0.89 ± 0.09	0.86 ± 0.09	0.87 ± 0.09	0.88 ± 0.09	0.89 ± 0.09	0.87 ± 0.09	0.87 ± 0.09
Systolic pulmonary arterial pressure	17.4 ± 1.3	17.3 ± 1.4	17.0 ± 1.4	17.3 ± 1.6	16.3 ± 1.8	17.1 ± 1.4	16.7 ± 1.4	17.2 ± 1.7	15.9 ± 1.8
Diastolic pulmonary arterial pressure	11.2 ± 0.7	11.1 ± 0.7	11.1 ± 0.7	11.1 ± 0.9	10.6 ± 0.9	11.0 ± 0.7	10.9 ± 0.7	11.0 ± 0.9	10.4 ± 0.9
Pulmonary vascular resistance	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013
Stroke volume	70 ± 7	70 ± 7	66 ± 7	71 ± 10	63 ± 10	69 ± 7	63 ± 7	70 ± 10	60 ± 10
Ejection fraction	64 ± 7	64 ± 7	63 ± 7	64 ± 7	61 ± 7	64 ± 7	62 ± 7	64 ± 7	60 ± 7
Cardiac output	5.3 ± 0.5	5.2 ± 0.5	5.2 ± 0.5	5.1 ± 0.5	5.0 ± 0.5	5.1 ± 0.5	5.2 ± 0.5	5.1 ± 0.5	4.9 ± 0.5
LV peak systolic pressure	172.4 ± 7.0	163.4 ± 7.4	153.1 ± 7.6	154.3 ± 9.4	148.2 ± 9.7	160.5 ± 7.5	149.6 ± 7.8	151.9 ± 10.1	144.4 ± 9.8
LV end-diastolic pressure	8.0 ± 1.1	8.1 ± 1.1	7.7 ± 1.1	8.2 ± 1.2	7.3 ± 1.2	8.0 ± 1.1	7.5 ± 1.1	8.1 ± 1.3	7.1 ± 1.2
LV end-systolic volume	40 ± 11	40 ± 11	40 ± 10	41 ± 11	40 ± 11	40 ± 11	40 ± 10	40 ± 11	40 ± 10
LV end-diastolic volume	110 ± 13	111 ± 14	105 ± 13	112 ± 15	103 ± 15	109 ± 14	103 ± 13	110 ± 16	100 ± 16
RV peak systolic pressure	19.6 ± 1.4	19.5 ± 1.4	19.2 ± 1.4	19.5 ± 1.7	18.4 ± 1.8	19.2 ± 1.4	18.9 ± 1.5	19.4 ± 1.7	17.9 ± 1.9
RV end-diastolic pressure	5.9 ± 1.1	6.0 ± 1.1	5.6 ± 1.0	6.0 ± 1.2	5.4 ± 1.2	5.9 ± 1.1	5.4 ± 1.0	5.9 ± 1.2	5.2 ± 1.1
RV end-systolic volume	47 ± 12	48 ± 12	46 ± 11	48 ± 12	46 ± 11	48 ± 12	46 ± 11	48 ± 12	46 ± 11
RV end-diastolic volume	117 ± 14	118 ± 14	112 ± 14	120 ± 17	109 ± 16	116 ± 14	109 ± 14	118 ± 17	106 ± 17
Aortic valve peak flow	564 ± 65	561 ± 67	539 ± 64	562 ± 78	513 ± 77	551 ± 67	524 ± 63	555 ± 80	497 ± 76
Pulmonary valve peak flow	542 ± 75	539 ± 77	524 ± 75	541 ± 86	498 ± 86	530 ± 76	511 ± 75	535 ± 88	483 ± 85
LV early peak filling rate	628 ± 124	641 ± 127	619 ± 120	664 ± 143	581 ± 135	627 ± 124	598 ± 116	654 ± 144	556 ± 131
LV active peak filling rate	418 ± 42	389 ± 42	343 ± 37	358 ± 47	332 ± 43	378 ± 42	330 ± 37	349 ± 48	318 ± 43
RV early peak filling rate	571 ± 100	586 ± 103	582 ± 99	611 ± 114	547 ± 111	577 ± 101	566 ± 97	605 ± 116	529 ± 109
RV active peak filling rate	529 ± 55	493 ± 54	435 ± 48	454 ± 58	425 ± 54	480 ± 53	421 ± 48	442 ± 59	409 ± 53
Glomerular filtration rate	0.097 ± 0.018	0.097 ± 0.018	0.106 ± 0.017	0.098 ± 0.019	0.093 ± 0.022	0.097 ± 0.018	0.106 ± 0.017	0.099 ± 0.019	0.093 ± 0.023
Renal blood flow	1.10 ± 0.15	1.19 ± 0.16	1.29 ± 0.17	1.20 ± 0.16	1.39 ± 0.19	1.19 ± 0.16	1.30 ± 0.17	1.20 ± 0.16	1.41 ± 0.19
Filtration fraction	0.16 ± 0.04	0.15 ± 0.04	0.15 ± 0.03	0.15 ± 0.04	0.12 ± 0.03	0.15 ± 0.04	0.15 ± 0.03	0.15 ± 0.04	0.12 ± 0.03
Filtration coefficient	0.010 ± 0.003	0.013 ± 0.004	0.013 ± 0.004	0.024 ± 0.007	0.011 ± 0.003	0.014 ± 0.004	0.014 ± 0.004	0.028 ± 0.009	0.012 ± 0.004
Renal vascular resistance	105.8 ± 14.2	91.0 ± 12.7	76.8 ± 10.7	82.4 ± 12.0	69.5 ± 9.5	88.7 ± 12.5	74.7 ± 10.5	80.8 ± 11.9	67.0 ± 9.3
Afferent arteriolar resistance	4842 ± 825	4093 ± 747	3158 ± 616	3683 ± 728	2833 ± 546	3980 ± 739	3054 ± 611	3605 ± 726	2702 ± 536
Efferent arteriolar resistance	2606 ± 458	2117 ± 377	1898 ± 338	1812 ± 324	1592 ± 282	2037 ± 364	1826 ± 326	1756 ± 314	1515 ± 269
Macula densa sodium flow rate	2.0 ± 0.8	1.9 ± 0.8	1.9 ± 0.8	1.9 ± 0.8	1.3 ± 0.5	1.9 ± 0.8	1.9 ± 0.8	1.9 ± 0.8	1.3 ± 0.5
Fractional proximal sodium reabsorption	0.86 ± 0.06	0.86 ± 0.06	0.87 ± 0.06	0.86 ± 0.06	0.89 ± 0.06	0.86 ± 0.06	0.87 ± 0.06	0.86 ± 0.06	0.89 ± 0.06
Fractional distal sodium reabsorption	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.92 ± 0.04	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.92 ± 0.04
Sodium	143.5 ± 1.3	143.5 ± 1.3	143.4 ± 1.3	143.4 ± 1.3	142.6 ± 1.3	143.4 ± 1.3	143.4 ± 1.3	143.4 ± 1.3	142.6 ± 1.3
Plasma renin activity	31.8 ± 3.6	12.7 ± 1.4	13.0 ± 1.5	3.8 ± 0.4	18.9 ± 2.1	9.9 ± 1.1	10.1 ± 1.2	3.0 ± 0.3	14.7 ± 1.7
Plasma renin concentration	33.1 ± 8.1	104.6 ± 25.6	107.2 ± 26.2	31.5 ± 7.7	155.6 ± 37.8	143.3 ± 35.1	146.9 ± 35.9	43.1 ± 10.6	213.1 ± 51.7
Plasma angiotensin I concentration	8.6 ± 1.0	3.4 ± 0.4	3.5 ± 0.4	1.0 ± 0.1	5.1 ± 0.6	2.7 ± 0.3	2.7 ± 0.3	0.8 ± 0.1	4.0 ± 0.4
Plasma angiotensin II concentration	5.4 ± 0.6	2.2 ± 0.2	2.2 ± 0.2	0.6 ± 0.1	3.2 ± 0.4	1.7 ± 0.2	1.7 ± 0.2	0.5 ± 0.1	2.5 ± 0.3
Plasma aldosterone concentration	182.4 ± 56.5	130.8 ± 40.5	131.9 ± 40.9	88.3 ± 27.4	138.4 ± 42.6	119.5 ± 37.0	120.6 ± 37.4	82.6 ± 25.6	126.2 ± 38.9

Table S7. Simulated effect of losartan 50 mg (L50), losartan 100 mg (L100), and their dual combinations with amlodipine 5 mg (A5), bisoprolol 5 mg (B5), and HCTZ 12.5 mg (H12.5) on model variables in the virtual population of hypertensive patients (n = 186) during 4 weeks of treatment, mean ± SD.

Parameters	**Baseline**	**L50**	**L50/A5**	**L50/B5**	**L50/H12.5**	**L100**	**L100/A5**	**L100/B5**	**L100/H12.5**
Total body water	37.3 ± 4.3	37.3 ± 4.3	37.0 ± 4.3	37.4 ± 4.3	36.8 ± 4.3	37.2 ± 4.3	36.7 ± 4.3	37.3 ± 4.3	36.5 ± 4.3
Systolic blood pressure	154 ± 7	146 ± 7	135 ± 7	137 ± 9	131 ± 9	141 ± 8	129 ± 8	133 ± 10	125 ± 9
Diastolic blood pressure	101 ± 6	93 ± 6	85 ± 5	84 ± 6	84 ± 5	90 ± 5	83 ± 5	81 ± 6	81 ± 5
Heart rate	76 ± 7	74 ± 8	80 ± 8	72 ± 8	81 ± 11	76 ± 8	83 ± 8	74 ± 9	85 ± 12
Systemic vascular resistance	0.89 ± 0.09	0.88 ± 0.09	0.89 ± 0.09	0.86 ± 0.09	0.87 ± 0.09	0.87 ± 0.09	0.89 ± 0.09	0.87 ± 0.09	0.87 ± 0.09
Systolic pulmonary arterial pressure	17.4 ± 1.3	17.3 ± 1.4	17.0 ± 1.4	17.4 ± 1.6	16.3 ± 1.8	16.9 ± 1.4	16.5 ± 1.4	17.2 ± 1.7	15.6 ± 1.8
Diastolic pulmonary arterial pressure	11.2 ± 0.7	11.1 ± 0.7	11.1 ± 0.7	11.1 ± 0.9	10.6 ± 0.9	10.9 ± 0.7	10.8 ± 0.8	11.0 ± 0.9	10.3 ± 0.9
Pulmonary vascular resistance	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013
Stroke volume	70 ± 7	70 ± 7	66 ± 7	71 ± 10	63 ± 10	68 ± 7	62 ± 8	70 ± 11	58 ± 11
Ejection fraction	64 ± 7	64 ± 7	63 ± 7	64 ± 7	61 ± 7	63 ± 7	61 ± 7	64 ± 7	60 ± 7
Cardiac output	5.3 ± 0.5	5.2 ± 0.5	5.2 ± 0.5	5.1 ± 0.5	5.0 ± 0.5	5.1 ± 0.5	5.1 ± 0.5	5.1 ± 0.5	4.8 ± 0.5
LV peak systolic pressure	172.4 ± 7.0	163.6 ± 7.4	153.3 ± 7.5	154.4 ± 9.4	148.4 ± 9.7	158.9 ± 7.6	147.6 ± 8.0	150.8 ± 10.5	142.3 ± 9.9
LV end-diastolic pressure	8.0 ± 1.1	8.1 ± 1.1	7.7 ± 1.1	8.2 ± 1.2	7.4 ± 1.2	7.9 ± 1.1	7.3 ± 1.1	8.0 ± 1.3	6.9 ± 1.2
LV end-systolic volume	40 ± 11	40 ± 11	40 ± 10	41 ± 11	40 ± 11	40 ± 11	40 ± 10	40 ± 11	40 ± 10
LV end-diastolic volume	110 ± 13	111 ± 14	106 ± 13	112 ± 15	103 ± 15	108 ± 14	102 ± 13	110 ± 16	98 ± 16
RV peak systolic pressure	19.6 ± 1.4	19.5 ± 1.4	19.2 ± 1.4	19.5 ± 1.7	18.4 ± 1.8	19.1 ± 1.4	18.6 ± 1.5	19.3 ± 1.8	17.7 ± 1.9
RV end-diastolic pressure	5.9 ± 1.1	6.0 ± 1.1	5.6 ± 1.0	6.1 ± 1.2	5.4 ± 1.2	5.8 ± 1.1	5.3 ± 1.0	5.9 ± 1.2	5.1 ± 1.1
RV end-systolic volume	47 ± 12	48 ± 12	46 ± 11	48 ± 12	46 ± 11	47 ± 12	46 ± 11	48 ± 12	45 ± 11
RV end-diastolic volume	117 ± 14	118 ± 14	112 ± 14	120 ± 17	109 ± 16	115 ± 14	108 ± 14	117 ± 18	104 ± 17
Aortic valve peak flow	564 ± 65	561 ± 67	540 ± 64	563 ± 78	514 ± 77	545 ± 66	516 ± 63	552 ± 81	487 ± 76
Pulmonary valve peak flow	542 ± 75	540 ± 77	524 ± 75	541 ± 86	499 ± 86	525 ± 76	503 ± 74	533 ± 89	474 ± 85
LV early peak filling rate	628 ± 124	641 ± 127	620 ± 120	664 ± 143	582 ± 135	619 ± 123	584 ± 114	651 ± 147	541 ± 129
LV active peak filling rate	418 ± 42	389 ± 42	343 ± 37	359 ± 47	332 ± 43	371 ± 42	324 ± 37	344 ± 49	311 ± 43
RV early peak filling rate	571 ± 100	587 ± 103	582 ± 99	611 ± 114	548 ± 111	572 ± 100	556 ± 96	604 ± 118	517 ± 108
RV active peak filling rate	529 ± 55	493 ± 54	436 ± 48	455 ± 58	425 ± 54	473 ± 53	413 ± 48	437 ± 60	400 ± 53
Glomerular filtration rate	0.097 ± 0.018	0.097 ± 0.018	0.106 ± 0.017	0.098 ± 0.019	0.093 ± 0.022	0.097 ± 0.018	0.106 ± 0.017	0.099 ± 0.019	0.094 ± 0.023
Renal blood flow	1.10 ± 0.15	1.19 ± 0.16	1.29 ± 0.17	1.20 ± 0.16	1.39 ± 0.19	1.20 ± 0.16	1.30 ± 0.17	1.20 ± 0.16	1.41 ± 0.19
Filtration fraction	0.16 ± 0.04	0.15 ± 0.04	0.15 ± 0.03	0.15 ± 0.04	0.12 ± 0.03	0.15 ± 0.04	0.15 ± 0.03	0.15 ± 0.04	0.12 ± 0.03
Filtration coefficient	0.010 ± 0.003	0.013 ± 0.004	0.016 ± 0.004	0.023 ± 0.007	0.011 ± 0.003	0.015 ± 0.005	0.015 ± 0.005	0.031 ± 0.010	0.013 ± 0.004
Renal vascular resistance	105.8 ± 14.2	91.1 ± 12.7	76.9 ± 10.7	82.4 ± 12.0	69.6 ± 9.5	87.6 ± 12.4	73.6 ± 10.5	79.8 ± 11.8	65.8 ± 9.2
Afferent arteriolar resistance	4842 ± 825	4098 ± 747	3162 ± 617	3686 ± 728	2839 ± 547	3928 ± 737	3005 ± 609	3557 ± 723	2640 ± 533
Efferent arteriolar resistance	2606 ± 458	2121 ± 378	1901 ± 338	1815 ± 325	1595 ± 282	1999 ± 357	1791 ± 320	1723 ± 307	1480 ± 264
Macula densa sodium flow rate	2.0 ± 0.8	1.9 ± 0.8	1.9 ± 0.8	1.9 ± 0.8	1.3 ± 0.5	1.9 ± 0.8	1.9 ± 0.8	1.9 ± 0.8	1.3 ± 0.5
Fractional proximal sodium reabsorption	0.86 ± 0.06	0.86 ± 0.06	0.87 ± 0.06	0.86 ± 0.06	0.89 ± 0.06	0.86 ± 0.06	0.87 ± 0.06	0.86 ± 0.06	0.89 ± 0.06
Fractional distal sodium reabsorption	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.92 ± 0.04	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.92 ± 0.04
Sodium	143.5 ± 1.3	143.5 ± 1.3	143.5 ± 1.3	143.4 ± 1.3	142.6 ± 1.3	143.4 ± 1.3	143.4 ± 1.3	143.4 ± 1.3	142.6 ± 1.3
Plasma renin activity	31.8 ± 3.6	99.2 ± 11.3	101.6 ± 11.5	29.9 ± 3.4	147.5 ± 16.6	163.3 ± 18.6	167.5 ± 19.0	49.1 ± 5.7	243.1 ± 27.5
Plasma renin concentration	33.1 ± 8.1	103.3 ± 25.3	105.8 ± 25.9	31.1 ± 7.6	153.6 ± 37.3	170.1 ± 41.7	174.5 ± 42.7	51.1 ± 12.5	253.1 ± 61.4
Plasma angiotensin I concentration	8.6 ± 1.0	26.7 ± 3.0	27.4 ± 3.1	8.0 ± 0.9	39.8 ± 4.5	44.0 ± 5.0	45.1 ± 5.1	13.2 ± 1.5	65.5 ± 7.4
Plasma angiotensin II concentration	5.4 ± 0.6	19.1 ± 2.2	19.5 ± 2.2	5.7 ± 0.7	28.4 ± 3.2	31.7 ± 3.6	32.5 ± 3.7	9.5 ± 1.1	47.2 ± 5.3
Plasma aldosterone concentration	182.4 ± 56.5	131.3 ± 40.7	132.4 ± 41.1	88.5 ± 27.5	138.9 ± 42.8	113.9 ± 35.3	114.9 ± 35.6	79.9 ± 24.8	120.1 ± 37.0

Table S8. Simulated effect of enalapril 20 mg (L100) and its dual combinations with amlodipine 5 mg (A5), bisoprolol 5 mg (B5), and HCTZ 12.5 mg (H12.5) on model variables in the virtual population of hypertensive patients (n = 186) during 4 weeks of treatment, mean ± SD.

Parameters	Baseline	E20	E20/A5	E20/B5	E20/H12.5
Total body water	37.3 ± 4.3	37.1 ± 4.3	36.6 ± 4.3	37.2 ± 4.3	36.3 ± 4.3
Systolic blood pressure	154 ± 7	139 ± 8	126 ± 8	131 ± 11	122 ± 10
Diastolic blood pressure	101 ± 6	89 ± 5	81 ± 5	80 ± 6	80 ± 5
Heart rate	76 ± 7	77 ± 8	86 ± 9	75 ± 10	88 ± 13
Systemic vascular resistance	0.89 ± 0.09	0.87 ± 0.09	0.89 ± 0.09	0.87 ± 0.09	0.87 ± 0.09
Systolic pulmonary arterial pressure	17.4 ± 1.3	16.7 ± 1.4	16.1 ± 1.5	17.2 ± 1.8	15.2 ± 1.9
Diastolic pulmonary arterial pressure	11.2 ± 0.7	10.8 ± 0.7	10.7 ± 0.8	11.1 ± 1.0	10.1 ± 1.0
Pulmonary vascular resistance	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013	0.100 ± 0.013
Stroke volume	70 ± 7	66 ± 8	59 ± 8	69 ± 12	55 ± 11
Ejection fraction	64 ± 7	63 ± 7	60 ± 7	63 ± 7	59 ± 7
Cardiac output	5.3 ± 0.5	5.1 ± 0.5	5.1 ± 0.5	5.1 ± 0.6	4.8 ± 0.5
LV peak systolic pressure	172.4 ± 7.0	156.3 ± 7.9	144.4 ± 8.4	149.1 ± 11.3	138.8 ± 10.1
LV end-diastolic pressure	8.0 ± 1.1	7.7 ± 1.1	7.1 ± 1.1	8.0 ± 1.3	6.7 ± 1.2
LV end-systolic volume	40 ± 11	40 ± 11	39 ± 10	40 ± 11	39 ± 10
LV end-diastolic volume	110 ± 13	106 ± 14	99 ± 14	109 ± 17	95 ± 16
RV peak systolic pressure	19.6 ± 1.4	18.9 ± 1.4	18.3 ± 1.6	19.3 ± 1.9	17.2 ± 2.0
RV end-diastolic pressure	5.9 ± 1.1	5.7 ± 1.1	5.2 ± 1.0	5.9 ± 1.2	4.9 ± 1.1
RV end-systolic volume	47 ± 12	47 ± 12	45 ± 11	48 ± 12	45 ± 11
RV end-diastolic volume	117 ± 14	113 ± 14	105 ± 14	117 ± 18	100 ± 17
Aortic valve peak flow	564 ± 65	535 ± 66	501 ± 64	551 ± 85	469 ± 75
Pulmonary valve peak flow	542 ± 75	516 ± 76	489 ± 75	532 ± 92	459 ± 85
LV early peak filling rate	628 ± 124	605 ± 120	562 ± 113	652 ± 153	516 ± 125
LV active peak filling rate	418 ± 42	361 ± 42	312 ± 38	337 ± 50	299 ± 42
RV early peak filling rate	571 ± 100	562 ± 98	538 ± 96	607 ± 123	498 ± 106
RV active peak filling rate	529 ± 55	461 ± 53	400 ± 48	427 ± 61	386 ± 52
Glomerular filtration rate	0.097 ± 0.018	0.097 ± 0.018	0.106 ± 0.017	0.100 ± 0.019	0.094 ± 0.023
Renal blood flow	1.10 ± 0.15	1.20 ± 0.16	1.30 ± 0.17	1.21 ± 0.16	1.42 ± 0.19
Filtration fraction	0.16 ± 0.04	0.15 ± 0.04	0.15 ± 0.03	0.15 ± 0.04	0.12 ± 0.03
Filtration coefficient	0.010 ± 0.003	0.017 ± 0.005	0.016 ± 0.005	0.037 ± 0.012	0.014 ± 0.004
Renal vascular resistance	105.8 ± 14.2	86.0 ± 12.3	72.1 ± 10.4	77.9 ± 11.7	64.0 ± 9.1
Afferent arteriolar resistance	4842 ± 825	3852 ± 734	2932 ± 608	3464 ± 719	2549 ± 529
Efferent arteriolar resistance	2606 ± 458	1942 ± 348	1739 ± 311	1662 ± 295	1428 ± 255
Macula densa sodium flow rate	2.0 ± 0.8	1.9 ± 0.8	1.9 ± 0.8	1.9 ± 0.8	1.3 ± 0.5
Fractional proximal sodium reabsorption	0.86 ± 0.06	0.86 ± 0.06	0.87 ± 0.06	0.86 ± 0.06	0.89 ± 0.06
Fractional distal sodium reabsorption	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.94 ± 0.03	0.92 ± 0.04
Sodium	143.5 ± 1.3	143.4 ± 1.3	143.4 ± 1.3	143.4 ± 1.3	142.6 ± 1.3
Plasma renin activity	31.8 ± 3.6	217.7 ± 24.9	223.4 ± 25.4	65.4 ± 7.5	324.0 ± 36.7
Plasma renin concentration	33.1 ± 8.1	226.7 ± 55.5	232.6 ± 56.9	68.1 ± 16.7	337.3 ± 81.9
Plasma angiotensin I concentration	8.6 ± 1.0	77.4 ± 8.8	79.4 ± 9.0	23.3 ± 2.7	115.2 ± 13.0
Plasma angiotensin II concentration	5.4 ± 0.6	1.2 ± 0.1	1.2 ± 0.1	0.3 ± 0.04	1.7 ± 0.2
Plasma aldosterone concentration	182.4 ± 56.5	105.4 ± 32.7	106.3 ± 33.0	75.9 ± 23.6	110.5 ± 34.0

Table S9. Correlation coefficients of virtual population parameters with reduction of systolic blood pressure in simulated treatment with aliskiren 150 mg (A150) and 300 mg (A300), amlodipine 5 mg (A5), bisoprolol 5 mg (B5), enalapril 20 mg (E20), HCTZ 12.5 mg (H12.5), losartan 100 mg (L100) and 50 mg (L50), and combinations of these drugs.

Parameters	**A150**	**A150 A5**	**A150 B5**	**A150 H12.5**	**A300**	**A300 A5**	**A300 B5**	**A300 H12.5**	**A5**	**B5**	**E20**	**E20 A5**	**E20 B5**	**E20 H12.5**	**H12.5**	**L100**	**L100 A5**	**L100 B5**	**L100 H12.5**	**L50**	**L50 A5**	**L50 B5**	**L50 H12.5**
General characteristics																							
Body mass index	-0.11	-0.08	-0.16	-0.02	-0.14	-0.11	-0.16	-0.04	0.01	-0.11	-0.16	-0.14	-0.16	-0.07	0.01	-0.14	-0.13	-0.16	-0.05	-0.11	-0.08	-0.16	-0.02
Total body water	-0.02	-0.05	-0.03	-0.09	-0.02	-0.06	-0.03	-0.09	-0.04	-0.02	-0.03	-0.06	-0.03	-0.10	-0.08	-0.03	-0.06	-0.03	-0.10	-0.02	-0.05	-0.03	-0.09
Sodium intake	-0.13	-0.04	-0.12	0.20	-0.09	-0.02	-0.11	0.20	0.10	-0.23	-0.05	0.00	-0.11	0.20	0.26	-0.07	-0.01	-0.11	0.20	-0.13	-0.04	-0.12	0.20
Water intake	0.02	0.08	0.03	0.00	0.02	0.07	0.03	0.00	0.12	0.01	0.03	0.06	0.03	0.01	0.00	0.02	0.07	0.03	0.01	0.02	0.08	0.02	0.00
Total exchangeable sodium	0.01	0.01	-0.02	0.01	0.00	-0.01	-0.02	0.00	0.03	0.00	-0.01	-0.02	-0.02	-0.01	0.02	-0.01	-0.02	-0.02	0.00	0.01	0.01	-0.02	0.01
Body oxygen demand	-0.02	-0.05	-0.08	0.02	-0.03	-0.05	-0.09	0.02	-0.02	-0.05	-0.05	-0.06	-0.11	0.00	0.02	-0.04	-0.06	-0.10	0.01	-0.02	-0.05	-0.08	0.02
Total metabolic intensity	0.26	0.29	0.24	0.13	0.26	0.30	0.24	0.15	0.09	0.20	0.25	0.28	0.24	0.18	0.06	0.26	0.30	0.24	0.16	0.26	0.29	0.24	0.13
Systemic hemodynamics																							
Systolic blood pressure	-0.07	0.07	-0.12	0.10	-0.04	0.06	-0.10	0.10	0.30	-0.28	0.00	0.07	-0.09	0.12	0.16	-0.02	0.06	-0.10	0.11	-0.08	0.07	-0.12	0.10
Diastolic blood pressure	-0.25	-0.38	-0.34	-0.12	-0.31	-0.45	-0.35	-0.18	0.01	-0.13	-0.37	-0.49	-0.37	-0.26	0.02	-0.34	-0.47	-0.36	-0.21	-0.24	-0.38	-0.33	-0.12
Heart rate	0.03	-0.17	0.02	-0.05	0.00	-0.16	0.00	-0.06	-0.23	0.12	-0.03	-0.15	-0.02	-0.07	-0.04	-0.01	-0.16	-0.01	-0.06	0.03	-0.17	0.02	-0.05
Systemic arterial tone	0.20	0.22	0.18	0.13	0.18	0.20	0.17	0.13	0.13	0.21	0.16	0.17	0.16	0.14	0.08	0.18	0.19	0.16	0.14	0.20	0.23	0.18	0.13
Sympathetic sensitivity of microvessels	-0.16	0.08	-0.10	0.11	-0.08	0.12	-0.06	0.14	0.18	-0.38	0.01	0.18	-0.02	0.19	0.14	-0.04	0.15	-0.04	0.16	-0.17	0.08	-0.10	0.11
Basic systemic arterial elasticity	0.07	0.22	0.09	0.10	0.13	0.27	0.11	0.14	0.14	-0.16	0.19	0.30	0.13	0.20	0.06	0.16	0.28	0.12	0.16	0.06	0.22	0.09	0.09
Basic systemic venous elasticity	0.03	0.10	0.05	0.17	0.05	0.10	0.05	0.18	0.12	-0.02	0.07	0.11	0.06	0.19	0.17	0.06	0.10	0.06	0.18	0.03	0.10	0.05	0.17
Systemic vascular resistance	-0.09	0.02	-0.04	-0.02	-0.05	0.04	-0.02	0.00	0.11	-0.19	0.00	0.06	0.00	0.02	0.01	-0.03	0.05	-0.01	0.01	-0.09	0.02	-0.04	-0.02
Pulmonary hemodynamics																							
Systolic blood pressure	0.01	-0.02	0.02	-0.09	0.00	-0.03	0.02	-0.10	0.00	0.06	-0.01	-0.04	0.03	-0.10	-0.09	0.00	-0.04	0.03	-0.10	0.01	-0.02	0.02	-0.09
Diastolic blood pressure	0.00	-0.03	0.00	-0.03	-0.01	-0.04	0.00	-0.04	0.00	0.03	-0.02	-0.06	0.00	-0.05	-0.02	-0.01	-0.05	0.00	-0.05	0.00	-0.02	0.00	-0.03
Basic pulmonary arterial elasticity	-0.02	-0.06	0.01	-0.10	-0.02	-0.05	0.01	-0.11	-0.06	0.02	-0.02	-0.05	0.02	-0.11	-0.10	-0.02	-0.05	0.02	-0.11	-0.02	-0.06	0.01	-0.10
Basic pulmonary venous elasticity	0.08	0.00	0.09	0.05	0.06	0.00	0.08	0.04	-0.03	0.12	0.05	0.00	0.08	0.04	0.06	0.06	0.00	0.08	0.04	0.08	0.00	0.09	0.05
Pulmonary vascular resistance	-0.02	-0.01	0.03	-0.09	0.01	0.01	0.04	-0.08	0.00	-0.05	0.03	0.03	0.06	-0.07	-0.09	0.02	0.02	0.05	-0.08	-0.02	-0.01	0.03	-0.09
Left ventricle (LV)																							
Stroke volume	-0.08	0.02	-0.11	-0.02	-0.08	-0.01	-0.10	-0.03	0.15	-0.09	-0.09	-0.04	-0.10	-0.04	0.01	-0.09	-0.02	-0.10	-0.04	-0.08	0.02	-0.11	-0.02
Ejection fraction	-0.02	0.00	-0.01	0.00	-0.01	0.00	-0.01	0.00	0.02	-0.04	0.00	0.00	-0.01	-0.01	0.00	-0.01	0.00	-0.01	0.00	-0.02	0.00	-0.01	0.00
Cardiac output	-0.06	-0.18	-0.10	-0.07	-0.10	-0.20	-0.11	-0.09	-0.10	0.04	-0.13	-0.21	-0.12	-0.13	-0.03	-0.11	-0.21	-0.12	-0.11	-0.06	-0.17	-0.10	-0.07
LV peak systolic pressure	-0.06	0.01	-0.11	0.08	-0.04	0.00	-0.10	0.07	0.22	-0.20	-0.03	0.00	-0.10	0.08	0.14	-0.04	-0.01	-0.10	0.07	-0.06	0.01	-0.11	0.08
LV end-diastolic pressure	0.00	0.05	0.02	0.02	0.01	0.04	0.02	0.02	0.04	0.00	0.01	0.03	0.03	0.02	0.02	0.01	0.04	0.03	0.02	0.00	0.05	0.02	0.02
LV end-systolic volume	-0.01	0.00	-0.02	-0.01	-0.02	-0.01	-0.02	-0.01	0.03	0.01	-0.03	-0.02	-0.03	-0.02	-0.01	-0.02	-0.01	-0.03	-0.02	-0.01	0.00	-0.02	-0.01
LV end-diastolic volume	-0.04	0.01	-0.07	-0.02	-0.06	-0.01	-0.07	-0.03	0.10	-0.04	-0.07	-0.03	-0.07	-0.04	0.00	-0.06	-0.02	-0.07	-0.03	-0.04	0.01	-0.07	-0.02
LV wall elasticity	0.02	0.03	0.03	-0.01	0.03	0.03	0.03	-0.01	-0.03	0.00	0.04	0.04	0.03	0.00	-0.03	0.03	0.04	0.03	0.00	0.02	0.03	0.03	-0.01
LV inotropic state	0.03	0.06	0.03	0.07	0.04	0.07	0.04	0.08	0.00	-0.01	0.05	0.08	0.04	0.10	0.06	0.04	0.08	0.04	0.09	0.03	0.06	0.03	0.07
Right ventricle (RV)																							
RV peak systolic pressure	0.02	-0.02	0.03	-0.08	0.01	-0.04	0.02	-0.09	-0.01	0.07	-0.01	-0.05	0.03	-0.10	-0.08	0.00	-0.04	0.03	-0.09	0.02	-0.02	0.03	-0.08
RV end-diastolic pressure	0.06	0.08	0.04	0.00	0.06	0.09	0.04	0.01	0.02	0.01	0.07	0.10	0.04	0.03	-0.03	0.06	0.09	0.04	0.02	0.05	0.08	0.04	0.00
RV end-systolic volume	0.01	0.02	0.01	0.06	0.01	0.02	0.01	0.06	0.02	0.01	0.01	0.03	0.02	0.06	0.06	0.01	0.02	0.02	0.06	0.01	0.02	0.01	0.06
RV end-diastolic volume	-0.03	0.03	-0.04	0.04	-0.03	0.01	-0.04	0.04	0.09	-0.03	-0.03	0.00	-0.03	0.03	0.05	-0.03	0.01	-0.03	0.03	-0.03	0.03	-0.04	0.04
RV wall elasticity	0.03	0.02	0.03	-0.06	0.03	0.04	0.03	-0.05	-0.03	0.00	0.04	0.05	0.03	-0.04	-0.07	0.04	0.04	0.03	-0.05	0.03	0.02	0.03	-0.06
RV inotropic state	0.04	0.10	0.01	-0.02	0.04	0.09	0.01	-0.02	0.08	0.02	0.03	0.06	0.00	-0.02	-0.05	0.04	0.08	0.00	-0.02	0.04	0.10	0.01	-0.02

Parameters	**A150**	**A150 A5**	**A150 B5**	**A150 H12.5**	**A300**	**A300 A5**	**A300 B5**	**A300 H12.5**	**A5**	**B5**	**E20**	**E20 A5**	**E20 B5**	**E20 H12.5**	**H12.5**	**L100**	**L100 A5**	**L100 B5**	**L100 H12.5**	**L50**	**L50 A5**	**L50 B5**	**L50 H12.5**
Peak flow rates through heart valves																							
Aortic valve peak flow	0.02	0.19	0.02	0.08	0.07	0.21	0.04	0.11	0.18	-0.18	0.12	0.23	0.05	0.15	0.06	0.09	0.22	0.05	0.13	0.02	0.19	0.02	0.08
Pulmonary valve peak flow	-0.05	-0.06	-0.06	-0.12	-0.07	-0.08	-0.06	-0.13	-0.01	0.00	-0.08	-0.10	-0.05	-0.15	-0.11	-0.07	-0.09	-0.05	-0.14	-0.05	-0.06	-0.06	-0.12
LV early peak filling rate	0.04	0.03	0.06	0.00	0.04	0.03	0.06	0.00	-0.03	0.05	0.04	0.03	0.06	0.00	-0.02	0.04	0.03	0.06	0.00	0.04	0.03	0.06	0.00
LV active peak filling rate	-0.23	-0.16	-0.28	-0.06	-0.25	-0.22	-0.28	-0.09	0.14	-0.22	-0.28	-0.26	-0.28	-0.14	0.04	-0.26	-0.24	-0.28	-0.11	-0.23	-0.16	-0.28	-0.05
RV early peak filling rate	0.05	0.06	0.05	0.02	0.06	0.07	0.06	0.02	0.00	0.02	0.07	0.08	0.05	0.04	0.00	0.07	0.08	0.05	0.03	0.05	0.06	0.05	0.02
RV active peak filling rate	-0.20	-0.14	-0.28	-0.05	-0.23	-0.19	-0.28	-0.08	0.14	-0.22	-0.25	-0.23	-0.29	-0.12	0.03	-0.24	-0.21	-0.28	-0.10	-0.20	-0.13	-0.28	-0.05
Renal hemodynamics																							
Glomerular filtration rate	0.26	0.47	0.24	0.05	0.26	0.43	0.23	0.07	0.45	0.20	0.25	0.37	0.22	0.11	-0.01	0.26	0.41	0.23	0.09	0.26	0.47	0.24	0.05
Renal blood flow	0.32	0.14	0.35	-0.03	0.32	0.17	0.35	-0.01	-0.10	0.29	0.32	0.21	0.36	0.03	-0.09	0.32	0.19	0.35	0.00	0.31	0.13	0.35	-0.03
Filtration fraction	0.06	0.32	-0.01	0.11	0.04	0.25	-0.02	0.11	0.44	0.03	0.03	0.17	-0.04	0.11	0.09	0.04	0.22	-0.03	0.11	0.06	0.32	-0.01	0.11
Filtration coefficient	-0.45	-0.03	-0.59	0.05	-0.50	-0.16	-0.60	0.00	0.43	-0.42	-0.55	-0.29	-0.60	-0.08	0.12	-0.52	-0.21	-0.60	-0.03	-0.45	-0.02	-0.59	0.05
Renal vascular resistance	-0.40	-0.22	-0.45	0.02	-0.41	-0.28	-0.46	-0.01	0.16	-0.38	-0.41	-0.32	-0.47	-0.07	0.12	-0.41	-0.29	-0.46	-0.03	-0.39	-0.22	-0.45	0.02
Number of nephrons	0.03	0.02	0.00	-0.01	0.03	0.03	-0.01	0.00	0.02	-0.01	0.03	0.03	-0.01	0.01	-0.02	0.03	0.03	-0.01	0.00	0.03	0.02	0.00	-0.01
Afferent arteriole diameter	0.55	0.52	0.64	0.42	0.59	0.57	0.65	0.47	0.07	0.49	0.62	0.59	0.66	0.53	0.29	0.61	0.58	0.65	0.49	0.55	0.52	0.64	0.42
Efferent arteriole diameter	0.17	0.16	0.17	0.06	0.16	0.15	0.17	0.07	0.02	0.19	0.14	0.14	0.17	0.08	0.00	0.15	0.15	0.17	0.07	0.17	0.16	0.17	0.06
Afferent arteriole length	0.00	0.00	-0.02	0.05	-0.01	-0.01	-0.02	0.04	0.04	0.03	-0.03	-0.03	-0.02	0.02	0.05	-0.02	-0.02	-0.02	0.03	0.00	0.01	-0.02	0.05
Efferent arteriole length	-0.06	-0.01	-0.07	0.04	-0.05	0.00	-0.07	0.04	0.05	-0.11	-0.03	0.00	-0.07	0.05	0.05	-0.04	0.00	-0.07	0.04	-0.06	-0.01	-0.07	0.04
Afferent arteriolar resistance	-0.46	-0.24	-0.55	0.01	-0.49	-0.31	-0.56	-0.03	0.22	-0.44	-0.51	-0.38	-0.57	-0.10	0.13	-0.50	-0.34	-0.56	-0.06	-0.46	-0.23	-0.55	0.01
Efferent arteriolar resistance	-0.22	-0.18	-0.19	-0.03	-0.20	-0.18	-0.18	-0.04	0.00	-0.22	-0.18	-0.16	-0.19	-0.06	0.05	-0.19	-0.17	-0.18	-0.05	-0.22	-0.18	-0.19	-0.03
Renal venous resistance	0.14	0.19	0.11	0.15	0.14	0.18	0.10	0.16	0.12	0.10	0.14	0.16	0.09	0.17	0.10	0.14	0.17	0.10	0.17	0.14	0.19	0.11	0.15
Renal venous pressure	0.04	0.03	0.00	-0.03	0.01	0.00	-0.01	-0.04	0.04	0.09	-0.02	-0.03	-0.02	-0.06	-0.03	0.00	-0.01	-0.01	-0.05	0.04	0.03	0.00	-0.03
Glomerular hydrostatic pressure	0.35	0.04	0.44	-0.02	0.38	0.11	0.44	0.01	-0.21	0.31	0.41	0.19	0.45	0.05	-0.04	0.40	0.14	0.45	0.02	0.35	0.03	0.44	-0.02
Glomerular capillary oncotic pressure	-0.22	-0.21	-0.28	-0.04	-0.23	-0.25	-0.28	-0.07	0.00	-0.22	-0.25	-0.28	-0.28	-0.11	0.03	-0.24	-0.26	-0.28	-0.08	-0.21	-0.21	-0.28	-0.04
Bowman's space hydrostatic pressure	-0.14	-0.15	-0.13	0.08	-0.14	-0.16	-0.13	0.05	-0.04	-0.09	-0.15	-0.17	-0.13	0.02	0.12	-0.15	-0.17	-0.13	0.04	-0.14	-0.15	-0.13	0.08
Macula densa sodium flow rate	0.08	0.43	0.05	0.76	0.09	0.35	0.04	0.75	0.62	0.01	0.09	0.25	0.03	0.71	0.79	0.09	0.31	0.04	0.73	0.08	0.43	0.05	0.76
Fractional proximal sodium reabsorption	0.04	-0.23	0.06	-0.74	0.03	-0.17	0.06	-0.71	-0.44	0.08	0.03	-0.09	0.07	-0.65	-0.79	0.03	-0.14	0.06	-0.69	0.04	-0.24	0.06	-0.74
Fractional distal sodium reabsorption	0.22	0.53	0.18	0.61	0.20	0.44	0.17	0.59	0.62	0.22	0.17	0.31	0.16	0.56	0.58	0.19	0.39	0.16	0.58	0.22	0.54	0.18	0.61
Blood parameters																							
Hematocrit	0.08	0.06	-0.01	0.10	0.05	0.03	-0.03	0.09	0.05	0.08	0.01	0.00	-0.04	0.07	0.08	0.04	0.02	-0.03	0.09	0.08	0.06	-0.01	0.10
Hemoglobin	-0.10	-0.09	-0.07	-0.11	-0.10	-0.09	-0.07	-0.12	-0.01	-0.06	-0.10	-0.09	-0.05	-0.12	-0.09	-0.10	-0.09	-0.06	-0.12	-0.10	-0.08	-0.07	-0.11
Sodium	0.14	0.33	0.07	0.56	0.13	0.27	0.05	0.55	0.40	0.11	0.10	0.18	0.03	0.51	0.56	0.12	0.23	0.05	0.54	0.14	0.33	0.07	0.56
Potassium	-0.08	0.00	-0.11	0.04	-0.09	-0.03	-0.11	0.03	0.08	-0.07	-0.10	-0.06	-0.12	0.01	0.05	-0.10	-0.04	-0.12	0.02	-0.08	0.00	-0.11	0.04
Glucose	0.08	0.12	0.10	0.00	0.10	0.13	0.11	0.02	0.01	0.04	0.11	0.14	0.11	0.05	-0.03	0.11	0.14	0.11	0.03	0.08	0.11	0.10	0.00
Total protein	-0.21	-0.29	-0.25	-0.06	-0.22	-0.30	-0.24	-0.09	-0.13	-0.20	-0.23	-0.30	-0.24	-0.13	0.00	-0.23	-0.30	-0.24	-0.11	-0.21	-0.29	-0.25	-0.06
Urea	-0.19	-0.10	-0.11	-0.05	-0.16	-0.09	-0.09	-0.05	0.05	-0.18	-0.12	-0.08	-0.08	-0.05	0.01	-0.14	-0.09	-0.08	-0.05	-0.19	-0.10	-0.11	-0.04
Blood viscosity	0.08	0.07	-0.02	0.11	0.05	0.04	-0.04	0.10	0.06	0.08	0.01	-0.01	-0.06	0.08	0.09	0.03	0.02	-0.04	0.09	0.08	0.07	-0.02	0.11
Arterial oxygen content	-0.10	-0.07	-0.07	-0.08	-0.10	-0.07	-0.06	-0.08	0.01	-0.08	-0.09	-0.06	-0.04	-0.08	-0.06	-0.09	-0.07	-0.05	-0.08	-0.10	-0.07	-0.07	-0.08
Venous oxygen content	-0.09	-0.07	-0.03	-0.10	-0.09	-0.08	-0.01	-0.11	0.00	-0.02	-0.08	-0.07	0.01	-0.11	-0.08	-0.09	-0.08	-0.01	-0.11	-0.09	-0.07	-0.03	-0.10
Arterial oxygen saturation	-0.06	-0.03	-0.06	0.05	-0.04	-0.01	-0.05	0.05	0.01	-0.14	-0.02	0.01	-0.05	0.06	0.06	-0.03	0.00	-0.05	0.06	-0.06	-0.03	-0.06	0.05
Oxygen capacity of hemoglobin	0.07	0.14	0.11	0.12	0.09	0.15	0.11	0.13	0.09	0.05	0.11	0.16	0.12	0.15	0.09	0.09	0.16	0.11	0.14	0.07	0.14	0.11	0.12

Parameters	**A150**	**A150 A5**	**A150 B5**	**A150 H12.5**	**A300**	**A300 A5**	**A300 B5**	**A300 H12.5**	**A5**	**B5**	**E20**	**E20 A5**	**E20 B5**	**E20 H12.5**	**H12.5**	**L100**	**L100 A5**	**L100 B5**	**L100 H12.5**	**L50**	**L50 A5**	**L50 B5**	**L50 H12.5**
Renin–angiotensin–aldosterone system																							
Plasma renin activity	-0.11	-0.13	0.15	-0.17	-0.02	-0.04	0.19	-0.14	-0.10	-0.10	0.09	0.06	0.22	-0.08	-0.12	0.03	0.00	0.21	-0.12	-0.12	-0.13	0.15	-0.17
Plasma renin concentration	-0.11	-0.17	-0.03	-0.15	-0.09	-0.14	-0.02	-0.15	-0.17	-0.07	-0.06	-0.09	-0.01	-0.14	-0.13	-0.07	-0.12	-0.02	-0.15	-0.11	-0.18	-0.03	-0.15
Plasma angiotensin I concentration	-0.11	-0.13	0.15	-0.17	-0.02	-0.04	0.19	-0.14	-0.10	-0.10	0.09	0.06	0.22	-0.08	-0.12	0.03	0.00	0.21	-0.12	-0.12	-0.13	0.15	-0.17
Plasma angiotensin II concentration	-0.11	-0.13	0.15	-0.17	-0.02	-0.04	0.19	-0.14	-0.10	-0.10	0.09	0.06	0.22	-0.08	-0.12	0.03	0.00	0.21	-0.12	-0.12	-0.13	0.15	-0.17
Plasma aldosterone concentration	0.02	0.10	0.01	0.12	0.01	0.07	0.01	0.11	0.15	0.04	0.00	0.04	0.01	0.10	0.11	0.00	0.06	0.01	0.11	0.02	0.10	0.01	0.12
Hormones																							
Plasma antidiuretic hormone	0.07	0.39	0.04	0.69	0.08	0.31	0.04	0.68	0.56	0.01	0.08	0.22	0.02	0.64	0.72	0.08	0.28	0.03	0.66	0.07	0.39	0.04	0.69
Plasma atrial natriuretic peptide	0.15	0.06	0.12	0.00	0.14	0.07	0.11	0.01	-0.08	0.15	0.12	0.06	0.10	0.02	-0.04	0.13	0.07	0.11	0.01	0.15	0.06	0.12	0.00

Table S10. Correlation coefficients of virtual population parameters with reduction of diastolic blood pressure in simulated treatment with aliskiren 150 mg (A150) and 300 mg (A300), amlodipine 5 mg (A5), bisoprolol 5 mg (B5), enalapril 20 mg (E20), HCTZ 12.5 mg (H12.5), losartan 100 mg (L100) and 50 mg (L50), and combinations of these drugs.

Parameters	A150	A150 A5	A150 B5	A150 H12.5	A300	A300 A5	A300 B5	A300 H12.5	A5	B5	E20	E20 A5	E20 B5	E20 H12.5	H12.5	L100	L100 A5	L100 B5	L100 H12.5	L50	L50 A5	L50 B5	L50 H12.5
General characteristics																							
Body mass index	-0.10	-0.10	-0.10	0.00	-0.10	-0.09	-0.10	0.00	-0.01	-0.06	-0.10	-0.08	-0.11	0.00	0.06	-0.10	-0.09	-0.10	0.00	-0.10	-0.10	-0.10	0.00
Total body water	-0.04	-0.03	-0.05	-0.06	-0.05	-0.03	-0.06	-0.05	0.02	-0.03	-0.04	-0.03	-0.05	-0.05	-0.02	-0.05	-0.03	-0.05	-0.05	-0.04	-0.03	-0.05	-0.06
Sodium intake	0.01	0.00	-0.01	0.15	-0.04	-0.06	-0.04	0.10	0.08	0.14	-0.09	-0.14	-0.07	0.03	0.20	-0.06	-0.09	-0.06	0.08	0.01	0.01	-0.01	0.16
Water intake	0.12	0.18	0.14	0.09	0.13	0.18	0.14	0.09	0.12	0.10	0.13	0.16	0.14	0.09	0.05	0.13	0.17	0.14	0.09	0.12	0.18	0.14	0.09
Total exchangeable sodium	-0.06	-0.01	-0.06	0.01	-0.06	-0.02	-0.06	0.01	0.08	-0.04	-0.06	-0.02	-0.05	0.00	0.06	-0.06	-0.02	-0.06	0.01	-0.06	-0.01	-0.06	0.01
Body oxygen demand	-0.11	0.04	-0.14	-0.06	-0.13	-0.01	-0.15	-0.08	0.21	-0.07	-0.14	-0.05	-0.13	-0.10	0.01	-0.13	-0.03	-0.14	-0.09	-0.11	0.04	-0.14	-0.06
Total metabolic intensity	-0.01	-0.07	0.03	-0.03	-0.01	-0.05	0.04	-0.02	-0.11	0.02	0.01	-0.02	0.05	0.00	-0.04	0.00	-0.04	0.04	-0.01	-0.01	-0.07	0.03	-0.03
Systemic hemodynamics																							
Systolic blood pressure	0.34	0.38	0.35	0.23	0.28	0.28	0.31	0.17	0.37	0.49	0.21	0.14	0.27	0.09	0.19	0.25	0.23	0.29	0.14	0.34	0.38	0.35	0.23
Diastolic blood pressure	0.23	0.48	0.15	0.33	0.25	0.44	0.15	0.32	0.60	0.05	0.25	0.37	0.14	0.30	0.35	0.25	0.41	0.15	0.31	0.23	0.48	0.15	0.33
Heart rate	-0.06	0.04	-0.06	0.04	-0.03	0.05	-0.03	0.05	0.09	-0.15	0.01	0.08	0.01	0.07	0.07	-0.02	0.06	-0.01	0.06	-0.06	0.04	-0.06	0.04
Systemic arterial tone	0.02	0.11	0.07	0.10	0.05	0.13	0.09	0.12	0.11	-0.02	0.09	0.16	0.12	0.15	0.09	0.06	0.14	0.10	0.13	0.02	0.11	0.07	0.10
Sympathetic sensitivity of microvessels	0.16	-0.21	0.16	-0.03	0.07	-0.28	0.10	-0.10	-0.29	0.44	-0.04	-0.37	0.02	-0.20	-0.03	0.03	-0.32	0.06	-0.14	0.16	-0.20	0.17	-0.03
Basic systemic arterial elasticity	0.10	-0.03	0.16	-0.03	0.06	-0.07	0.14	-0.06	-0.11	0.33	0.00	-0.11	0.12	-0.10	-0.06	0.03	-0.08	0.13	-0.07	0.10	-0.03	0.17	-0.02
Basic systemic venous elasticity	0.04	0.00	0.03	0.11	0.03	-0.01	0.01	0.09	-0.02	0.09	0.01	-0.04	-0.02	0.07	0.11	0.02	-0.02	0.00	0.08	0.04	0.00	0.03	0.11
Systemic vascular resistance	0.28	0.14	0.29	0.12	0.25	0.13	0.26	0.10	-0.04	0.35	0.21	0.09	0.21	0.07	0.02	0.24	0.11	0.24	0.09	0.28	0.14	0.29	0.12
Pulmonary hemodynamics																							
Systolic blood pressure	0.08	0.05	0.06	-0.05	0.10	0.07	0.06	-0.03	-0.03	0.01	0.11	0.09	0.04	0.00	-0.10	0.10	0.08	0.05	-0.02	0.08	0.05	0.06	-0.05
Diastolic blood pressure	0.04	0.09	0.03	0.06	0.05	0.10	0.04	0.08	0.08	0.00	0.07	0.11	0.04	0.09	0.05	0.06	0.11	0.04	0.08	0.04	0.09	0.03	0.06
Basic pulmonary arterial elasticity	0.07	-0.03	0.05	-0.08	0.08	0.00	0.05	-0.06	-0.14	0.01	0.09	0.03	0.03	-0.03	-0.13	0.08	0.01	0.04	-0.04	0.07	-0.04	0.05	-0.08
Basic pulmonary venous elasticity	0.07	0.08	0.09	0.11	0.09	0.11	0.10	0.13	0.01	0.01	0.12	0.13	0.11	0.15	0.10	0.10	0.12	0.11	0.14	0.07	0.08	0.09	0.11
Pulmonary vascular resistance	0.22	0.08	0.20	-0.01	0.21	0.09	0.18	0.00	-0.13	0.21	0.19	0.09	0.15	0.01	-0.12	0.21	0.09	0.17	0.00	0.22	0.08	0.20	-0.01
Left ventricle (LV)																							
Stroke volume	-0.06	-0.04	-0.06	-0.05	-0.07	-0.06	-0.08	-0.06	0.06	-0.01	-0.08	-0.08	-0.09	-0.08	-0.01	-0.07	-0.07	-0.08	-0.07	-0.06	-0.04	-0.06	-0.05
Ejection fraction	0.01	-0.06	0.01	-0.03	0.01	-0.05	0.01	-0.03	-0.09	0.04	0.00	-0.05	-0.01	-0.03	-0.05	0.00	-0.05	0.00	-0.03	0.01	-0.06	0.01	-0.03
Cardiac output	-0.14	0.00	-0.14	0.00	-0.12	0.00	-0.13	0.00	0.16	-0.19	-0.09	0.00	-0.10	0.00	0.08	-0.11	0.00	-0.12	0.00	-0.14	0.00	-0.14	0.00
LV peak systolic pressure	0.29	0.38	0.29	0.21	0.25	0.29	0.26	0.17	0.40	0.37	0.19	0.16	0.24	0.09	0.19	0.23	0.24	0.25	0.14	0.29	0.38	0.29	0.22
LV end-diastolic pressure	-0.01	-0.03	-0.01	0.01	-0.01	-0.02	-0.01	0.02	-0.05	0.00	0.00	-0.01	-0.01	0.03	0.01	-0.01	-0.01	-0.01	0.02	-0.01	-0.03	0.00	0.01
LV end-systolic volume	-0.03	0.05	-0.04	0.01	-0.03	0.04	-0.04	0.01	0.12	-0.05	-0.03	0.02	-0.03	0.00	0.04	-0.03	0.03	-0.03	0.01	-0.03	0.05	-0.04	0.01
LV end-diastolic volume	-0.06	0.02	-0.07	-0.02	-0.06	0.00	-0.07	-0.02	0.13	-0.05	-0.07	-0.02	-0.07	-0.04	0.03	-0.06	-0.01	-0.07	-0.03	-0.06	0.02	-0.07	-0.02
LV wall elasticity	-0.02	-0.07	-0.01	-0.03	-0.02	-0.06	-0.01	-0.03	-0.09	0.01	-0.02	-0.04	-0.01	-0.02	-0.03	-0.02	-0.05	-0.01	-0.03	-0.02	-0.07	-0.01	-0.03
LV inotropic state	-0.07	-0.16	-0.07	-0.04	-0.08	-0.15	-0.07	-0.04	-0.17	-0.02	-0.09	-0.15	-0.08	-0.05	-0.03	-0.08	-0.15	-0.08	-0.05	-0.07	-0.16	-0.07	-0.04
Right ventricle (RV)																							
RV peak systolic pressure	0.06	0.06	0.04	-0.05	0.08	0.08	0.04	-0.03	0.01	-0.02	0.09	0.09	0.03	0.00	-0.09	0.08	0.08	0.04	-0.02	0.06	0.06	0.04	-0.05
RV end-diastolic pressure	0.00	-0.02	-0.02	-0.10	-0.02	-0.03	-0.02	-0.11	0.00	0.02	-0.04	-0.05	-0.02	-0.11	-0.10	-0.03	-0.04	-0.02	-0.11	0.00	-0.01	-0.02	-0.10
RV end-systolic volume	-0.04	-0.03	-0.04	0.01	-0.04	-0.04	-0.04	0.00	0.00	-0.03	-0.04	-0.04	-0.03	-0.01	0.03	-0.04	-0.04	-0.04	0.00	-0.04	-0.03	-0.04	0.01
RV end-diastolic volume	-0.06	-0.04	-0.06	-0.02	-0.07	-0.06	-0.07	-0.03	0.03	-0.04	-0.08	-0.07	-0.07	-0.04	0.02	-0.07	-0.06	-0.07	-0.03	-0.06	-0.04	-0.06	-0.02
RV wall elasticity	-0.01	-0.04	-0.02	-0.08	-0.01	-0.04	-0.02	-0.08	-0.06	0.01	-0.02	-0.04	-0.03	-0.07	-0.09	-0.02	-0.04	-0.02	-0.08	-0.01	-0.04	-0.02	-0.08
RV inotropic state	-0.06	-0.01	-0.06	-0.06	-0.06	-0.02	-0.06	-0.06	0.04	-0.04	-0.06	-0.02	-0.07	-0.05	-0.04	-0.06	-0.02	-0.06	-0.05	-0.06	-0.01	-0.06	-0.06

Parameters	**A150**	**A150 A5**	**A150 B5**	**A150 H12.5**	**A300**	**A300 A5**	**A300 B5**	**A300 H12.5**	**A5**	**B5**	**E20**	**E20 A5**	**E20 B5**	**E20 H12.5**	**H12.5**	**L100**	**L100 A5**	**L100 B5**	**L100 H12.5**	**L50**	**L50 A5**	**L50 B5**	**L50 H12.5**
Peak flow rates through heart valves																							
Aortic valve peak flow	0.02	-0.08	0.08	-0.05	-0.03	-0.12	0.05	-0.09	-0.08	0.25	-0.08	-0.18	0.03	-0.14	-0.05	-0.05	-0.14	0.04	-0.11	0.02	-0.08	0.08	-0.05
Pulmonary valve peak flow	-0.01	-0.05	-0.03	-0.10	0.00	-0.03	-0.03	-0.08	-0.05	-0.05	0.01	-0.01	-0.05	-0.07	-0.10	0.00	-0.02	-0.04	-0.08	-0.01	-0.05	-0.03	-0.10
LV early peak filling rate	-0.06	-0.10	-0.04	-0.05	-0.05	-0.08	-0.04	-0.04	-0.09	-0.04	-0.04	-0.05	-0.03	-0.03	-0.03	-0.05	-0.06	-0.03	-0.04	-0.06	-0.10	-0.04	-0.05
LV active peak filling rate	0.05	0.15	0.02	0.16	0.05	0.12	0.01	0.15	0.26	0.06	0.04	0.07	-0.02	0.12	0.21	0.04	0.10	0.00	0.14	0.05	0.15	0.02	0.16
RV early peak filling rate	-0.08	-0.08	-0.09	-0.11	-0.09	-0.10	-0.10	-0.12	-0.03	-0.04	-0.10	-0.11	-0.10	-0.13	-0.08	-0.10	-0.10	-0.10	-0.12	-0.08	-0.08	-0.09	-0.11
RV active peak filling rate	0.04	0.18	0.00	0.13	0.03	0.13	-0.02	0.10	0.33	0.07	0.01	0.07	-0.04	0.06	0.18	0.02	0.10	-0.02	0.09	0.04	0.18	0.00	0.13
Renal hemodynamics																							
Glomerular filtration rate	0.24	0.45	0.28	0.11	0.25	0.43	0.29	0.13	0.42	0.19	0.26	0.37	0.30	0.15	0.02	0.26	0.41	0.29	0.14	0.24	0.45	0.27	0.11
Renal blood flow	0.34	0.26	0.36	0.13	0.37	0.30	0.38	0.16	-0.02	0.23	0.39	0.32	0.39	0.19	-0.01	0.38	0.31	0.38	0.18	0.34	0.26	0.36	0.13
Filtration fraction	-0.05	0.22	-0.04	0.04	-0.05	0.17	-0.03	0.03	0.42	-0.03	-0.05	0.11	-0.01	0.02	0.07	-0.05	0.15	-0.03	0.03	-0.05	0.23	-0.04	0.04
Filtration coefficient	-0.39	-0.08	-0.50	-0.04	-0.42	-0.16	-0.53	-0.08	0.34	-0.31	-0.46	-0.25	-0.56	-0.13	0.11	-0.44	-0.20	-0.54	-0.09	-0.38	-0.08	-0.50	-0.04
Renal vascular resistance	-0.21	-0.07	-0.25	0.01	-0.24	-0.14	-0.27	-0.04	0.23	-0.12	-0.28	-0.20	-0.29	-0.09	0.14	-0.26	-0.17	-0.28	-0.06	-0.21	-0.07	-0.25	0.01
Number of nephrons	0.10	0.10	0.06	0.06	0.08	0.08	0.05	0.05	0.07	0.09	0.05	0.04	0.04	0.03	0.01	0.07	0.06	0.04	0.04	0.10	0.10	0.06	0.06
Afferent arteriole diameter	0.21	0.04	0.29	0.16	0.24	0.11	0.31	0.19	-0.28	0.18	0.28	0.18	0.34	0.24	0.04	0.25	0.14	0.33	0.21	0.21	0.04	0.29	0.16
Efferent arteriole diameter	0.09	0.13	0.07	0.08	0.10	0.16	0.08	0.10	0.04	0.00	0.13	0.18	0.08	0.12	0.02	0.11	0.17	0.08	0.11	0.09	0.13	0.07	0.08
Afferent arteriole length	-0.02	0.01	-0.04	0.01	-0.01	0.01	-0.04	0.01	0.05	-0.05	-0.01	0.00	-0.05	0.01	0.02	-0.01	0.00	-0.05	0.01	-0.02	0.01	-0.04	0.01
Efferent arteriole length	-0.03	-0.08	-0.02	-0.04	-0.05	-0.10	-0.02	-0.06	-0.02	0.05	-0.08	-0.13	-0.02	-0.09	-0.01	-0.06	-0.11	-0.02	-0.08	-0.03	-0.08	-0.02	-0.04
Afferent arteriolar resistance	-0.23	-0.01	-0.28	0.05	-0.26	-0.09	-0.31	0.00	0.34	-0.14	-0.30	-0.18	-0.33	-0.06	0.19	-0.28	-0.13	-0.32	-0.02	-0.22	0.00	-0.28	0.05
Efferent arteriolar resistance	-0.15	-0.18	-0.11	-0.13	-0.16	-0.19	-0.11	-0.16	-0.04	-0.05	-0.17	-0.20	-0.11	-0.17	-0.04	-0.16	-0.20	-0.11	-0.17	-0.14	-0.17	-0.11	-0.13
Renal venous resistance	0.04	0.08	0.00	0.11	0.03	0.06	0.00	0.10	0.08	0.03	0.01	0.03	-0.01	0.08	0.09	0.02	0.04	-0.01	0.09	0.04	0.08	0.00	0.11
Renal venous pressure	-0.03	0.08	-0.07	0.03	-0.02	0.08	-0.07	0.05	0.13	-0.11	0.00	0.09	-0.07	0.06	0.04	-0.01	0.09	-0.07	0.05	-0.03	0.08	-0.07	0.03
Glomerular hydrostatic pressure	0.42	0.23	0.48	0.09	0.44	0.27	0.49	0.12	-0.10	0.33	0.47	0.29	0.50	0.14	-0.04	0.45	0.28	0.50	0.13	0.42	0.22	0.48	0.09
Glomerular capillary oncotic pressure	-0.12	-0.12	-0.18	-0.04	-0.14	-0.15	-0.20	-0.06	0.02	-0.07	-0.17	-0.19	-0.23	-0.10	0.04	-0.15	-0.17	-0.21	-0.08	-0.12	-0.12	-0.18	-0.04
Bowman's space hydrostatic pressure	-0.04	-0.04	-0.12	0.04	-0.05	-0.05	-0.14	0.03	-0.01	-0.07	-0.06	-0.06	-0.16	0.02	0.06	-0.05	-0.05	-0.14	0.02	-0.04	-0.04	-0.12	0.04
Macula densa sodium flow rate	0.07	0.30	0.12	0.61	0.07	0.25	0.12	0.56	0.45	0.14	0.06	0.17	0.12	0.51	0.67	0.06	0.22	0.12	0.54	0.07	0.31	0.12	0.61
Fractional proximal sodium reabsorption	0.03	-0.13	-0.01	-0.57	0.04	-0.08	0.00	-0.52	-0.28	-0.06	0.05	-0.03	0.01	-0.45	-0.67	0.04	-0.06	0.00	-0.49	0.03	-0.13	-0.01	-0.57
Fractional distal sodium reabsorption	0.09	0.36	0.16	0.49	0.11	0.34	0.18	0.49	0.44	0.05	0.15	0.32	0.21	0.48	0.52	0.13	0.33	0.19	0.49	0.08	0.36	0.16	0.49
Blood parameters																							
Hematocrit	-0.15	0.01	-0.16	-0.01	-0.15	-0.01	-0.15	-0.02	0.19	-0.16	-0.14	-0.03	-0.11	-0.02	0.06	-0.14	-0.02	-0.14	-0.02	-0.15	0.01	-0.16	-0.01
Hemoglobin	0.02	-0.01	0.01	0.01	0.02	0.01	0.01	0.01	-0.04	-0.01	0.03	0.02	0.00	0.01	-0.01	0.02	0.01	0.00	0.01	0.02	-0.01	0.01	0.01
Sodium	-0.10	0.13	-0.06	0.36	-0.09	0.09	-0.05	0.33	0.34	-0.06	-0.08	0.05	-0.02	0.30	0.46	-0.09	0.08	-0.04	0.32	-0.10	0.13	-0.06	0.36
Potassium	-0.14	-0.07	-0.15	-0.05	-0.15	-0.08	-0.15	-0.06	0.07	-0.12	-0.15	-0.09	-0.15	-0.06	0.01	-0.15	-0.09	-0.15	-0.06	-0.14	-0.07	-0.15	-0.05
Glucose	0.01	-0.05	0.03	0.01	0.01	-0.04	0.03	0.01	-0.10	0.05	0.01	-0.03	0.03	0.01	-0.02	0.01	-0.04	0.03	0.01	0.01	-0.05	0.03	0.01
Total protein	-0.10	-0.18	-0.15	-0.05	-0.11	-0.19	-0.17	-0.07	-0.11	-0.06	-0.14	-0.20	-0.20	-0.10	0.01	-0.12	-0.20	-0.18	-0.08	-0.10	-0.18	-0.15	-0.05
Urea	0.16	0.07	0.14	0.06	0.14	0.06	0.12	0.05	-0.04	0.18	0.12	0.03	0.08	0.03	0.00	0.13	0.05	0.11	0.05	0.16	0.07	0.14	0.06
Blood viscosity	-0.16	0.02	-0.17	0.00	-0.15	-0.01	-0.15	0.00	0.21	-0.17	-0.14	-0.03	-0.12	-0.01	0.08	-0.15	-0.02	-0.14	-0.01	-0.16	0.02	-0.17	0.00
Arterial oxygen content	0.02	-0.03	0.01	0.00	0.02	-0.02	0.01	0.00	-0.07	0.02	0.01	-0.02	0.00	0.00	-0.01	0.02	-0.02	0.00	0.00	0.02	-0.03	0.01	0.00
Venous oxygen content	0.06	-0.05	0.08	0.05	0.08	-0.01	0.08	0.06	-0.16	0.02	0.09	0.02	0.07	0.07	0.01	0.08	0.00	0.08	0.07	0.06	-0.05	0.08	0.05
Arterial oxygen saturation	-0.02	-0.10	-0.01	-0.06	-0.05	-0.13	-0.02	-0.09	-0.08	0.08	-0.08	-0.16	-0.02	-0.12	-0.04	-0.06	-0.14	-0.02	-0.10	-0.02	-0.10	-0.01	-0.06
Oxygen capacity of hemoglobin	0.03	-0.01	0.04	0.06	0.03	-0.01	0.04	0.06	-0.07	0.05	0.02	-0.01	0.03	0.05	0.03	0.03	-0.01	0.04	0.05	0.03	-0.01	0.04	0.06

Parameters	A150	A150 A5	A150 B5	A150 H12.5	A300	A300 A5	A300 B5	A300 H12.5	A5	B5	E20	E20 A5	E20 B5	E20 H12.5	H12.5	L100	L100 A5	L100 B5	L100 H12.5	L50	L50 A5	L50 B5	L50 H12.5
Renin–angiotensin–aldosterone system																							
Plasma renin activity	0.71	0.46	0.58	0.14	0.68	0.46	0.53	0.16	-0.13	0.61	0.61	0.40	0.45	0.17	-0.21	0.66	0.44	0.50	0.17	0.72	0.46	0.58	0.14
Plasma renin concentration	0.12	0.05	0.06	-0.09	0.11	0.05	0.06	-0.08	-0.08	0.08	0.09	0.04	0.04	-0.06	-0.18	0.10	0.05	0.05	-0.07	0.12	0.05	0.06	-0.09
Plasma angiotensin I concentration	0.71	0.46	0.58	0.14	0.68	0.46	0.53	0.16	-0.13	0.61	0.61	0.40	0.45	0.17	-0.21	0.66	0.44	0.50	0.17	0.72	0.46	0.58	0.14
Plasma angiotensin II concentration	0.71	0.46	0.58	0.14	0.68	0.46	0.53	0.16	-0.13	0.61	0.61	0.40	0.45	0.17	-0.21	0.66	0.44	0.50	0.17	0.72	0.46	0.58	0.14
Plasma aldosterone concentration	0.02	0.13	0.01	0.16	0.03	0.12	0.02	0.16	0.17	-0.01	0.04	0.11	0.02	0.16	0.17	0.03	0.11	0.02	0.16	0.02	0.13	0.01	0.16
Hormones																							
Plasma antidiuretic hormone	0.00	0.21	0.04	0.51	-0.01	0.15	0.04	0.47	0.37	0.07	-0.01	0.09	0.04	0.41	0.58	-0.01	0.13	0.04	0.45	0.00	0.21	0.04	0.51
Plasma atrial natriuretic peptide	-0.02	0.01	0.02	-0.05	0.00	0.02	0.04	-0.04	0.01	-0.05	0.02	0.05	0.07	-0.02	-0.04	0.01	0.03	0.05	-0.03	-0.02	0.00	0.02	-0.05

Table S11. Correlation coefficients of virtual population parameters with reduction of mean arterial pressure in simulated treatment with aliskiren 150 mg (A150) and 300 mg (A300), amlodipine 5 mg (A5), bisoprolol 5 mg (B5), enalapril 20 mg (E20), HCTZ 12.5 mg (H12.5), losartan 100 mg (L100) and 50 mg (L50), and combinations of these drugs.

Parameters	A150	A150 A5	A150 B5	A150 H12.5	A300	A300 A5	A300 B5	A300 H12.5	A5	B5	E20	E20 A5	E20 B5	E20 H12.5	H12.5	L100	L100 A5	L100 B5	L100 H12.5	L50	L50 A5	L50 B5	L50 H12.5
General characteristics																							
Body mass index	-0.14	-0.11	-0.16	-0.01	-0.15	-0.13	-0.16	-0.03	0.00	-0.14	-0.15	-0.15	-0.16	-0.05	0.03	-0.15	-0.14	-0.16	-0.04	-0.14	-0.11	-0.16	-0.01
Total body water	-0.04	-0.06	-0.04	-0.09	-0.04	-0.06	-0.04	-0.09	-0.01	-0.04	-0.05	-0.06	-0.04	-0.09	-0.06	-0.04	-0.06	-0.04	-0.09	-0.04	-0.06	-0.04	-0.09
Sodium intake	-0.08	-0.02	-0.09	0.21	-0.08	-0.05	-0.10	0.19	0.10	-0.08	-0.08	-0.08	-0.11	0.16	0.25	-0.08	-0.06	-0.10	0.18	-0.08	-0.02	-0.09	0.21
Water intake	0.09	0.16	0.08	0.04	0.09	0.15	0.07	0.04	0.14	0.09	0.08	0.14	0.07	0.05	0.02	0.09	0.15	0.07	0.04	0.09	0.16	0.08	0.04
Total exchangeable sodium	-0.03	0.00	-0.04	0.01	-0.04	-0.02	-0.04	0.00	0.06	-0.03	-0.04	-0.03	-0.04	0.00	0.03	-0.04	-0.02	-0.04	0.00	-0.03	0.00	-0.04	0.01
Body oxygen demand	-0.08	-0.01	-0.12	-0.01	-0.09	-0.04	-0.12	-0.02	0.10	-0.10	-0.10	-0.08	-0.13	-0.04	0.02	-0.10	-0.06	-0.13	-0.03	-0.08	-0.01	-0.12	-0.01
Total metabolic intensity	0.16	0.17	0.19	0.09	0.17	0.19	0.19	0.10	-0.01	0.18	0.17	0.21	0.20	0.13	0.03	0.17	0.20	0.19	0.12	0.16	0.17	0.19	0.09
Systemic hemodynamics																							
Systolic blood pressure	0.17	0.27	0.06	0.16	0.14	0.21	0.04	0.15	0.38	0.14	0.10	0.13	0.02	0.12	0.18	0.13	0.18	0.04	0.14	0.17	0.27	0.06	0.16
Diastolic blood pressure	-0.01	0.02	-0.18	0.04	-0.06	-0.08	-0.20	0.00	0.34	-0.06	-0.12	-0.17	-0.23	-0.06	0.15	-0.08	-0.12	-0.22	-0.02	-0.01	0.02	-0.18	0.05
Heart rate	-0.02	-0.10	-0.01	-0.02	-0.02	-0.09	-0.01	-0.02	-0.09	-0.01	-0.02	-0.07	-0.01	-0.02	0.00	-0.02	-0.08	-0.01	-0.02	-0.02	-0.10	-0.01	-0.02
Systemic arterial tone	0.14	0.22	0.16	0.13	0.15	0.23	0.16	0.15	0.13	0.15	0.15	0.22	0.16	0.17	0.09	0.15	0.22	0.16	0.15	0.14	0.22	0.16	0.13
Sympathetic sensitivity of microvessels	0.00	-0.07	0.00	0.07	-0.01	-0.07	-0.01	0.06	-0.05	0.02	-0.01	-0.07	-0.01	0.05	0.09	-0.01	-0.07	-0.01	0.06	0.00	-0.07	0.00	0.07
Basic systemic arterial elasticity	0.11	0.14	0.14	0.06	0.12	0.16	0.14	0.08	0.02	0.12	0.13	0.17	0.14	0.10	0.01	0.12	0.16	0.14	0.08	0.11	0.14	0.14	0.06
Basic systemic venous elasticity	0.05	0.07	0.05	0.17	0.05	0.07	0.04	0.17	0.06	0.05	0.05	0.06	0.04	0.17	0.16	0.05	0.07	0.04	0.17	0.05	0.07	0.05	0.17
Systemic vascular resistance	0.12	0.10	0.09	0.03	0.12	0.10	0.09	0.04	0.04	0.11	0.11	0.10	0.07	0.05	0.02	0.11	0.10	0.08	0.04	0.12	0.10	0.09	0.03
Pulmonary hemodynamics																							
Systolic blood pressure	0.06	0.02	0.04	-0.08	0.06	0.02	0.04	-0.08	-0.02	0.06	0.05	0.02	0.04	-0.08	-0.10	0.06	0.02	0.04	-0.08	0.06	0.02	0.04	-0.08
Diastolic blood pressure	0.03	0.04	0.02	0.00	0.02	0.03	0.01	0.00	0.04	0.03	0.02	0.02	0.01	0.00	0.00	0.02	0.02	0.01	0.00	0.03	0.04	0.02	0.00
Basic pulmonary arterial elasticity	0.03	-0.06	0.03	-0.10	0.03	-0.04	0.03	-0.10	-0.12	0.03	0.03	-0.02	0.03	-0.09	-0.12	0.03	-0.03	0.03	-0.10	0.03	-0.06	0.03	-0.10
Basic pulmonary venous elasticity	0.10	0.05	0.10	0.08	0.10	0.06	0.10	0.08	-0.01	0.10	0.10	0.07	0.10	0.09	0.07	0.10	0.06	0.10	0.09	0.10	0.05	0.10	0.08
Pulmonary vascular resistance	0.13	0.04	0.11	-0.07	0.13	0.06	0.10	-0.06	-0.07	0.12	0.12	0.07	0.10	-0.04	-0.11	0.13	0.07	0.10	-0.05	0.13	0.04	0.11	-0.07
Left ventricle (LV)																							
Stroke volume	-0.09	-0.01	-0.10	-0.03	-0.09	-0.04	-0.10	-0.05	0.12	-0.09	-0.10	-0.07	-0.10	-0.07	0.00	-0.10	-0.05	-0.10	-0.05	-0.09	0.00	-0.10	-0.03
Ejection fraction	0.00	-0.03	0.00	-0.02	0.00	-0.03	-0.01	-0.02	-0.04	0.00	0.00	-0.02	-0.01	-0.02	-0.01	0.00	-0.03	-0.01	-0.02	-0.01	-0.03	0.00	-0.02
Cardiac output	-0.13	-0.12	-0.13	-0.05	-0.13	-0.15	-0.13	-0.07	0.03	-0.12	-0.14	-0.16	-0.13	-0.09	0.01	-0.13	-0.16	-0.13	-0.08	-0.13	-0.12	-0.13	-0.05
LV peak systolic pressure	0.15	0.22	0.04	0.14	0.12	0.16	0.02	0.12	0.35	0.12	0.08	0.09	0.00	0.10	0.17	0.10	0.13	0.02	0.11	0.15	0.23	0.04	0.14
LV end-diastolic pressure	-0.01	0.02	0.01	0.02	0.00	0.02	0.02	0.03	0.00	0.00	0.01	0.02	0.02	0.03	0.02	0.00	0.02	0.02	0.03	-0.01	0.02	0.01	0.02
LV end-systolic volume	-0.03	0.03	-0.03	0.00	-0.03	0.01	-0.03	-0.01	0.08	-0.03	-0.03	0.00	-0.03	-0.01	0.01	-0.03	0.01	-0.03	-0.01	-0.03	0.03	-0.03	0.00
LV end-diastolic volume	-0.07	0.02	-0.08	-0.02	-0.07	-0.01	-0.08	-0.03	0.13	-0.07	-0.08	-0.04	-0.08	-0.04	0.01	-0.08	-0.02	-0.08	-0.03	-0.07	0.02	-0.08	-0.02
LV wall elasticity	0.00	-0.02	0.02	-0.02	0.01	-0.01	0.02	-0.02	-0.07	0.01	0.01	0.01	0.02	-0.01	-0.03	0.01	0.00	0.02	-0.01	0.00	-0.02	0.02	-0.02
LV inotropic state	-0.03	-0.05	0.00	0.04	-0.02	-0.04	0.00	0.04	-0.09	-0.02	-0.01	-0.02	0.00	0.05	0.03	-0.02	-0.03	0.00	0.04	-0.03	-0.05	0.00	0.04
Right ventricle (RV)																							
RV peak systolic pressure	0.06	0.02	0.03	-0.08	0.05	0.02	0.03	-0.08	0.00	0.05	0.04	0.01	0.03	-0.07	-0.09	0.05	0.01	0.03	-0.08	0.06	0.02	0.03	-0.08
RV end-diastolic pressure	0.03	0.05	0.02	-0.04	0.03	0.05	0.02	-0.04	0.01	0.03	0.03	0.05	0.02	-0.03	-0.06	0.03	0.05	0.02	-0.03	0.03	0.05	0.02	-0.04
RV end-systolic volume	-0.02	0.00	-0.01	0.05	-0.02	0.00	0.00	0.04	0.01	-0.02	-0.02	0.00	0.00	0.04	0.05	-0.02	0.00	0.00	0.04	-0.02	0.00	-0.01	0.05
RV end-diastolic volume	-0.06	-0.01	-0.05	0.02	-0.06	-0.02	-0.05	0.02	0.07	-0.05	-0.06	-0.04	-0.05	0.01	0.04	-0.06	-0.03	-0.05	0.01	-0.06	0.00	-0.05	0.02
RV wall elasticity	0.01	-0.01	0.02	-0.07	0.01	0.00	0.02	-0.07	-0.05	0.01	0.02	0.02	0.02	-0.06	-0.08	0.01	0.01	0.02	-0.07	0.01	-0.01	0.02	-0.07
RV inotropic state	-0.01	0.06	-0.02	-0.04	-0.01	0.05	-0.02	-0.04	0.07	-0.01	-0.01	0.04	-0.02	-0.03	-0.05	-0.01	0.05	-0.02	-0.04	-0.01	0.06	-0.02	-0.04

Parameters	A150	A150 A5	A150 B5	A150 H12.5	A300	A300 A5	A300 B5	A300 H12.5	A5	B5	E20	E20 A5	E20 B5	E20 H12.5	H12.5	L100	L100 A5	L100 B5	L100 H12.5	L50	L50 A5	L50 B5	L50 H12.5
Peak flow rates through heart valves																							
Aortic valve peak flow	0.03	0.09	0.05	0.04	0.03	0.09	0.05	0.04	0.06	0.04	0.04	0.08	0.05	0.05	0.02	0.03	0.08	0.05	0.05	0.03	0.09	0.05	0.04
Pulmonary valve peak flow	-0.04	-0.07	-0.05	-0.12	-0.04	-0.08	-0.05	-0.13	-0.03	-0.04	-0.05	-0.08	-0.05	-0.14	-0.11	-0.05	-0.08	-0.05	-0.13	-0.04	-0.07	-0.05	-0.12
LV early peak filling rate	-0.01	-0.03	0.02	-0.02	0.00	-0.02	0.03	-0.02	-0.07	0.01	0.01	0.00	0.03	-0.02	-0.02	0.00	-0.01	0.03	-0.02	-0.01	-0.04	0.02	-0.02
LV active peak filling rate	-0.11	-0.03	-0.19	0.02	-0.14	-0.09	-0.20	-0.01	0.22	-0.13	-0.17	-0.16	-0.22	-0.05	0.10	-0.15	-0.12	-0.21	-0.02	-0.11	-0.02	-0.19	0.02
RV early peak filling rate	-0.01	-0.01	0.00	-0.03	-0.01	0.00	0.00	-0.03	-0.02	-0.01	-0.01	0.00	0.00	-0.03	-0.03	-0.01	0.00	0.00	-0.03	-0.01	-0.01	0.00	-0.03
RV active peak filling rate	-0.10	0.01	-0.20	0.02	-0.13	-0.07	-0.21	-0.02	0.26	-0.13	-0.16	-0.14	-0.23	-0.06	0.09	-0.14	-0.10	-0.22	-0.03	-0.10	0.01	-0.20	0.02
Renal hemodynamics																							
Glomerular filtration rate	0.32	0.59	0.29	0.08	0.32	0.56	0.28	0.11	0.49	0.31	0.31	0.49	0.27	0.14	0.00	0.31	0.53	0.28	0.12	0.32	0.60	0.29	0.08
Renal blood flow	0.43	0.25	0.40	0.03	0.42	0.30	0.40	0.06	-0.07	0.42	0.42	0.34	0.40	0.11	-0.06	0.42	0.32	0.40	0.08	0.43	0.24	0.40	0.03
Filtration fraction	0.01	0.35	-0.02	0.09	0.00	0.28	-0.03	0.09	0.48	0.00	-0.01	0.20	-0.04	0.09	0.08	0.00	0.25	-0.03	0.09	0.01	0.36	-0.02	0.09
Filtration coefficient	-0.54	-0.07	-0.64	0.02	-0.57	-0.21	-0.64	-0.03	0.44	-0.58	-0.60	-0.36	-0.64	-0.11	0.12	-0.59	-0.27	-0.64	-0.06	-0.54	-0.06	-0.64	0.02
Renal vascular resistance	-0.40	-0.20	-0.43	0.02	-0.41	-0.28	-0.44	-0.03	0.22	-0.41	-0.42	-0.36	-0.45	-0.09	0.14	-0.41	-0.31	-0.44	-0.05	-0.39	-0.19	-0.43	0.02
Number of nephrons	0.08	0.08	0.02	0.02	0.07	0.06	0.01	0.02	0.05	0.06	0.05	0.04	0.01	0.02	-0.01	0.06	0.05	0.01	0.02	0.08	0.08	0.02	0.02
Afferent arteriole diameter	0.49	0.39	0.59	0.36	0.52	0.48	0.60	0.42	-0.11	0.54	0.56	0.55	0.61	0.49	0.21	0.54	0.51	0.60	0.45	0.49	0.38	0.59	0.36
Efferent arteriole diameter	0.17	0.19	0.16	0.07	0.16	0.20	0.16	0.09	0.04	0.16	0.16	0.21	0.16	0.11	0.01	0.16	0.21	0.16	0.10	0.17	0.19	0.16	0.07
Afferent arteriole length	-0.01	0.01	-0.03	0.04	-0.02	-0.01	-0.03	0.03	0.05	-0.02	-0.02	-0.02	-0.03	0.02	0.04	-0.02	-0.01	-0.03	0.03	-0.01	0.01	-0.03	0.04
Efferent arteriole length	-0.06	-0.05	-0.06	0.01	-0.06	-0.06	-0.06	0.01	0.02	-0.06	-0.06	-0.07	-0.06	-0.01	0.03	-0.06	-0.07	-0.06	0.00	-0.06	-0.05	-0.06	0.01
Afferent arteriolar resistance	-0.45	-0.17	-0.52	0.03	-0.47	-0.28	-0.53	-0.02	0.31	-0.47	-0.49	-0.39	-0.54	-0.10	0.16	-0.48	-0.33	-0.53	-0.05	-0.45	-0.17	-0.52	0.03
Efferent arteriolar resistance	-0.24	-0.23	-0.18	-0.07	-0.23	-0.24	-0.18	-0.09	-0.02	-0.22	-0.21	-0.24	-0.18	-0.12	0.01	-0.22	-0.24	-0.18	-0.10	-0.24	-0.23	-0.18	-0.07
Renal venous resistance	0.12	0.18	0.08	0.15	0.11	0.16	0.07	0.16	0.11	0.11	0.10	0.14	0.06	0.16	0.10	0.10	0.16	0.07	0.16	0.12	0.18	0.08	0.15
Renal venous pressure	0.00	0.07	-0.03	-0.01	-0.01	0.05	-0.03	-0.01	0.09	-0.01	-0.02	0.03	-0.04	-0.02	-0.01	-0.01	0.04	-0.04	-0.01	0.00	0.07	-0.03	-0.01
Glomerular hydrostatic pressure	0.50	0.16	0.52	0.02	0.51	0.23	0.51	0.05	-0.18	0.51	0.51	0.31	0.51	0.10	-0.04	0.51	0.27	0.51	0.07	0.50	0.15	0.52	0.02
Glomerular capillary oncotic pressure	-0.22	-0.22	-0.28	-0.04	-0.24	-0.27	-0.29	-0.07	0.01	-0.24	-0.26	-0.32	-0.29	-0.13	0.04	-0.24	-0.29	-0.29	-0.09	-0.22	-0.22	-0.28	-0.04
Bowman's space hydrostatic pressure	-0.11	-0.13	-0.15	0.07	-0.12	-0.15	-0.15	0.05	-0.03	-0.12	-0.13	-0.17	-0.15	0.02	0.11	-0.13	-0.16	-0.15	0.04	-0.11	-0.13	-0.15	0.07
Macula densa sodium flow rate	0.10	0.48	0.09	0.79	0.10	0.40	0.08	0.77	0.60	0.12	0.09	0.29	0.06	0.74	0.79	0.10	0.36	0.07	0.76	0.10	0.48	0.09	0.79
Fractional proximal sodium reabsorption	0.05	-0.24	0.04	-0.75	0.05	-0.17	0.05	-0.73	-0.41	0.02	0.04	-0.09	0.05	-0.68	-0.79	0.04	-0.14	0.05	-0.71	0.05	-0.24	0.04	-0.75
Fractional distal sodium reabsorption	0.20	0.58	0.19	0.63	0.20	0.52	0.19	0.63	0.60	0.22	0.19	0.42	0.19	0.62	0.59	0.19	0.48	0.19	0.63	0.20	0.59	0.19	0.63
Blood parameters																							
Hematocrit	-0.04	0.05	-0.07	0.07	-0.05	0.02	-0.07	0.06	0.13	-0.06	-0.06	-0.02	-0.07	0.04	0.08	-0.06	0.00	-0.07	0.05	-0.04	0.05	-0.07	0.07
Hemoglobin	-0.06	-0.06	-0.05	-0.08	-0.05	-0.06	-0.05	-0.08	-0.03	-0.05	-0.05	-0.06	-0.04	-0.08	-0.06	-0.05	-0.06	-0.04	-0.08	-0.05	-0.06	-0.05	-0.08
Sodium	0.03	0.31	0.03	0.54	0.03	0.25	0.02	0.53	0.42	0.04	0.03	0.17	0.02	0.51	0.55	0.03	0.22	0.02	0.52	0.03	0.31	0.03	0.55
Potassium	-0.14	-0.04	-0.14	0.01	-0.15	-0.07	-0.14	0.00	0.09	-0.15	-0.15	-0.10	-0.14	-0.02	0.04	-0.15	-0.08	-0.14	-0.01	-0.14	-0.04	-0.14	0.01
Glucose	0.06	0.05	0.09	0.01	0.07	0.07	0.09	0.02	-0.05	0.07	0.08	0.09	0.09	0.04	-0.03	0.07	0.08	0.09	0.03	0.06	0.05	0.09	0.01
Total protein	-0.20	-0.30	-0.24	-0.07	-0.21	-0.33	-0.25	-0.09	-0.13	-0.21	-0.23	-0.35	-0.25	-0.14	0.01	-0.22	-0.34	-0.25	-0.11	-0.20	-0.30	-0.24	-0.06
Urea	-0.02	-0.03	-0.02	-0.01	-0.02	-0.03	-0.02	-0.01	0.01	-0.01	-0.02	-0.04	-0.03	-0.02	0.00	-0.02	-0.04	-0.02	-0.02	-0.02	-0.03	-0.02	-0.01
Blood viscosity	-0.05	0.06	-0.08	0.08	-0.06	0.02	-0.08	0.07	0.15	-0.06	-0.07	-0.02	-0.08	0.05	0.09	-0.06	0.00	-0.08	0.06	-0.05	0.06	-0.08	0.08
Arterial oxygen content	-0.06	-0.06	-0.04	-0.06	-0.05	-0.06	-0.04	-0.06	-0.03	-0.05	-0.05	-0.06	-0.03	-0.06	-0.04	-0.05	-0.06	-0.04	-0.06	-0.06	-0.06	-0.04	-0.06
Venous oxygen content	-0.02	-0.08	0.01	-0.06	-0.01	-0.06	0.02	-0.05	-0.09	0.00	0.00	-0.04	0.03	-0.05	-0.05	-0.01	-0.05	0.02	-0.05	-0.02	-0.08	0.01	-0.06
Arterial oxygen saturation	-0.05	-0.08	-0.05	0.01	-0.05	-0.08	-0.05	0.00	-0.04	-0.05	-0.05	-0.08	-0.04	-0.01	0.03	-0.05	-0.08	-0.04	0.00	-0.05	-0.08	-0.05	0.01
Oxygen capacity of hemoglobin	0.06	0.09	0.10	0.11	0.07	0.11	0.10	0.12	0.01	0.08	0.08	0.12	0.10	0.13	0.07	0.08	0.11	0.10	0.12	0.06	0.09	0.10	0.11

Parameters	**A150**	**A150 A5**	**A150 B5**	**A150 H12.5**	**A300**	**A300 A5**	**A300 B5**	**A300 H12.5**	**A5**	**B5**	**E20**	**E20 A5**	**E20 B5**	**E20 H12.5**	**H12.5**	**L100**	**L100 A5**	**L100 B5**	**L100 H12.5**	**L50**	**L50 A5**	**L50 B5**	**L50 H12.5**
Renin–angiotensin–aldosterone system																							
Plasma renin activity	0.39	0.18	0.35	-0.07	0.39	0.23	0.34	-0.03	-0.13	0.38	0.38	0.27	0.32	0.02	-0.16	0.38	0.25	0.34	-0.02	0.39	0.18	0.36	-0.07
Plasma renin concentration	0.00	-0.09	0.01	-0.14	0.01	-0.07	0.01	-0.14	-0.14	0.00	0.01	-0.05	0.00	-0.13	-0.16	0.01	-0.06	0.01	-0.14	0.00	-0.09	0.01	-0.15
Plasma angiotensin I concentration	0.39	0.18	0.35	-0.07	0.39	0.23	0.34	-0.03	-0.13	0.38	0.38	0.27	0.32	0.02	-0.16	0.38	0.25	0.34	-0.02	0.39	0.18	0.36	-0.07
Plasma angiotensin II concentration	0.39	0.18	0.35	-0.07	0.39	0.23	0.34	-0.03	-0.13	0.38	0.38	0.27	0.32	0.02	-0.16	0.38	0.25	0.34	-0.02	0.39	0.18	0.36	-0.07
Plasma aldosterone concentration	0.02	0.14	0.01	0.15	0.02	0.12	0.01	0.15	0.18	0.02	0.02	0.09	0.01	0.14	0.14	0.02	0.11	0.01	0.15	0.02	0.15	0.01	0.15
Hormones																							
Plasma antidiuretic hormone	0.04	0.39	0.05	0.70	0.05	0.32	0.04	0.68	0.53	0.07	0.05	0.22	0.03	0.65	0.71	0.05	0.28	0.04	0.67	0.04	0.40	0.05	0.70
Plasma atrial natriuretic peptide	0.09	0.04	0.09	-0.02	0.09	0.06	0.10	-0.01	-0.04	0.09	0.09	0.08	0.10	0.00	-0.05	0.09	0.07	0.10	-0.01	0.09	0.04	0.09	-0.02

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