



HYPERTENSION

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2013 ESH/ESC Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

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European Heart Journal 2013

Journal of Hypertension 2013

Blood Pressure 2013

This calls for earlier intervention in the natural history of hypertension, before organ damage develops or when early damage can still be prevented.

The earlier the better

10 year risk of fatal CVD in low risk regions of Europe

		Wom	nen	0	Men	70101010
		Non-smoker	Smoker	Age	Non-smoker Smoker	
	180 4	4 5 6 6 7	9 9 11 12 14		8 9 10 12 14 15 17 20 23 26	
	160	3 3 4 4 5	6 6 7 8 10	65	5 6 7 8 10 10 12 14 16 19	
	140 2	2 2 2 3 3	4 4 5 6 7		4 4 5 6 7 7 8 9 11 13	
	120 1	1 1 2 2 2	3 3 3 4 4		2 3 3 4 5 5 5 6 8 9	SCORE
	180 3	3 3 3 4 4	5 5 6 7 8		5 6 7 8 9 10 11 13 15 18	15% and over
-	160 2	2 2 2 2 3	3 4 4 5 5	60	3 4 5 5 6 7 8 9 11 13	1578 and over
(p)	140 1	1 1 1 2 2	2 2 3 3 4		2 3 3 4 4 5 5 6 7 9	10%-14%
Ē	120 1	1 1 1 1 1	1 2 2 2 3		2 2 2 3 3 3 4 4 5 6	5%-9%
an	180 1	1 1 2 2 2	3 3 3 4 4		3 4 4 5 6 6 7 8 10 12	3%-4%
8	160 1	1 1 1 1 1	2 2 2 3 3	55	2 2 3 3 4 4 5 6 7 8	200
8	140 1	1 1 1 1 1	1 1 1 2 2	00	1 2 2 2 3 3 3 4 5 6	2%
	120	0 0 1 1 1	1 1 1 1 1		1 1 1 2 2 2 2 3 3 4	1%
stoli	180 1	1 1 1 1 1	1 1 2 2 2		2 2 3 3 4 4 4 5 6 7	< 1%
ŝ	160	0 0 1 1 1	1 1 1 1 1	50	1 1 2 2 2 2 3 3 4 5	
	140	0 0 0 0 0	1 1 1 1 1	50	1 1 1 1 2 2 2 2 3 3	
	120	0 0 0 0 0	00011		1 1 1 1 1 1 1 2 2 2 U	
	180	0 0 0 0 0	0 0 0 0 0			
	160	0 0 0 0 0	0 0 0 0 0	40	00011 11111	
	140	0 0 0 0 0	0 0 0 0 0	40	0000001111	
	120	0 0 0 0 0	00000		000000011 🔘	
	4	4 5 6 7 8	4 5 6 7 8		4 5 6 7 8 4 5 6 7 8	a france and the second
			Total ch	olesterol	mmoVL) 150 200 250 300	~



European Heart Journal 2012:33;1635–1701 European Journal of Preventive Cardiology 2012;19: 4:585-667

www.escardio.org/guidelines



Initiation Of Lifestyle Changes And Antihypertensive Drug Treatment

Other rick factors		Blood Press	ure (mmHg)	
asymptomatic organ damage or disease	High normal SBP 130–139 or DBP 85–89	Grade I HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF	• No BP intervention	 Lifestyle changes for several months Then add BP drugs targeting <140/90 	 Lifestyle changes for several weeks Then add BP drugs targeting <140/90 	 Lifestyle changes Immediate BP drugs targeting <140/90
I–2 RF	 Lifestyle changes No BP intervention 	 Lifestyle changes for several weeks Then add BP drugs targeting <140/90 	 Lifestyle changes for several weeks Then add BP drugs targeting <140/90 	 Lifestyle changes Immediate BP drugs targeting <140/90
≥3 RF	 Lifestyle changes No BP intervention 	 Lifestyle changes for several weeks Then add BP drugs targeting <140/90 	 Lifestyle changes BP drugs targeting <140/90 	 Lifestyle changes Immediate BP drugs targeting <140/90
OD, CKD stage 3 or diabetes	 Lifestyle changes No BP intervention 	 Lifestyle changes BP drugs targeting <140/90 	 Lifestyle changes BP drugs targeting <140/90 	 Lifestyle changes Immediate BP drugs targeting <140/90
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	 Lifestyle changes No BP intervention 	 Lifestyle changes BP drugs targeting <140/90 	 Lifestyle changes BP drugs targeting <140/90 	 Lifestyle changes Immediate BP drugs targeting <140/90



Initiation Of Drug Treatment In Hypertension

Grade 2-3	Recommended (Promptly)	IA
Grade 1 / High CV risk	Recommended	IB
Grade 1 / Low CV risk	Should be considered	llaB
Elderly	Recommended if SBP ≥ 160 mmHg (also > 80 ys of age)	IA
	May be considered if SBP 140-159 mmHg	llbC
High normal BP	No drug treatment recommended	IIIA

Blood pressure lowering treatment based on CV risk: a meta analysis



LANCET 2014;384:591-98. Blood pressure trialist collaboration

Blood pressure lowering treatment based on CV risk: a meta analysis



igure 3: Effects of blood pressure reduction on absolute and proportional risks of coronary heart disease, stroke, heart failure, cardiovascular mortality, and all-cause mortality for patient troups defined by different baseline levels of risk of those outcomes

LANCET 2014;384:591-98. Blood pressure trialist collaboration

Blood pressure lowering treatment based on CV risk: a meta analysis



LANCET 2014;384:591-98. Blood pressure trialist collaboration

Effects of blood pressure lowering on outcome incidence in hypertension: Effects in patients at different level of CV risk- meta analysis

	cv	Trials	Outcome risk	Difference SBP/DBP	E (n/p	vents atients)	Standardized RR	Standardized	P-value	Absolute risk reduction 1000 pts/5 years	NNT 5 years
Dutcome	risk	(n)	(% in 5 y)	(mmHg)	Treated	Controls	(95% C1)	RR (95% CI)	for trend	(95% CI)	(95% CI)
Stroka	Low-moderate	17	16	-63/-38	382/34666	599/40495	0.67 (0.53-0.83)		0.91	-5 (-7 -3)	185 (134 363)
Durone	High	8	4.6	-7.0/-3.6	501/99038	830/22105	0.59 (0.49-0.70)	-0-	0.01	-18 (-22 -13)	55 (45, 75)
	Very high	16	9.1	-6.2/-3.0	2429/45153	2917/44283	0.63 (0.52-0.75)	-0-		-31 (-39, -22)	32 (25, 46)
	Very very high	14	10.3	-8.5/-4.4	813/13833	943/12812	0.64 (0.51-0.80)			-34 (-45, -20)	29 (22, 51)
СНД	Low-moderate	19	1.7	-6.3/-3.9	607/35678	698/41066	0.90 (0.80-1.04)	-0-	0.49	-1 (-3, +1)	780 (289, -1440)
	High	8	6.4	-6.9/-3.5	1183/21387	1263/21266	0.88 (0.76-1.04)	-0-		-7 (-14, +1)	135 (68, -815)
	Very high	17	5.7	-6.1/-2.8	1749/45390	2070/44516	0.67 (0.57-0.78)	-0-		-18 (-23, -12)	55 (43, 81)
	Very very high	15	4.6	-8.5/-4.4	475/13891	467/12870	0.85 (0.65-1.11)	-+-		-6 (-16, +5)	166 (64, -194)
HF	Low-moderate	10	0.9	-5.5/-3.2	143/14214	149/13547	0.82 (0.44-1.57)		0.83	-1 (-5, +5)	806 (186, -203)
	High	4	3.0	-5.6/-2.8	333/15186	427/15213	0.63 (0.49-0.82)	-0		-11 (-15, -5)	92 (67, 187)
	Very high	11	5.3	-5.8/-2.5	1093/33019	1307/32199	0.60 (0.43-0.86)			-20 (-29, -10)	50 (37, 107)
	Very very high	11	14.0	-7.9/-4.0	1097/12554	1238/11989	0.57 (0.41-0.82)			-54 (-74, -34)	18 (14, 25)
Stroke + CHD	Low-moderate	19	3.3	-6.2/-3.8	1001/35609	1297/40706	0.81 (0.73-0.91)	-0-	0.70	-6 (-9, -3)	167 (112, 334)
	High	7	10.7	-6.9/-3.6	1732/20998	1988/21065	0.81 (0.71-0.94)	-0-		-18 (-30, -6)	56 (33, 157)
	Very high	16	14.7	-6.2/-3.0	4172/45153	4973/44283	0.67 (0.59-0.76)	-0-		-46 (-56, -34)	22 (18, 29)
	Very very high	15	14,9	-8.5/-4.3	1288/13891	1410/12870	0.71 (0.60-0.84)			-41 (-55, -25)	24 (18, 41)
Stroke + CHD + HF	Low-moderate	10	4.1	-8.1/-4.3	847/22356	957/21648	0.84 (0.76-0.93)	~	0.76	-7 (-10, -3)	152 (101, 362)
	High	4	13.2	-5.6/-2.8	1539/15186	1773/15213	0.75 (0.61-0.93)			-30 (-50, -9)	33 (20, 108)
	Very high	12	19.2	-6.3/-2.8	4376/35202	5033/34412	0.69 (0.57-0.81)	-0-		-56 (-76, -35)	18 (13, 28)
	Very very high	12	30.5	-7.9/-4.0	2345/12614	2601/12049	0.69 (0.59-0.82)	-		-87 (-112, -62)	11 (9, 16)
CV death	Low-moderate	19	1.3	-6.2/-3.8	463/35609	508/40706	1.19 (0.86-1.65)		0.69	+3 (-2, +8)	
	High	8	3.5	-7.1/-3.6	604/21298	684/21375	0.83 (0.69-0.98)	-0-		-6 (-10, -1)	166 (98, 852)
	Very high	17	6.7	-6.3/-3.1	2022/45583	2276/44690	0.76 (0.68-0.86)	-0-		-15 (-20, -9)	64 (49, 109)
	Very very high	15	16.1	-8.5/-4.4	1488/13891	1498/12870	0.80 (0.64-0.98)	-		-28 (-54, -3)	32 (19, 312)
All-cause death	Low-moderate	21	3.0	-6.2/-3.8	1031/36936	1221/42633	1.00 (0.88-1.14)	+	0.79	0 (-4, +4)	
	High	11	6.7	-7.1/-3.7	1318/23135	1439/23027	0.87 (0.76-1.00)		11 11.00	-9 (-17, 0)	114 (59, ∞)
	Very high	19	12.7	-6.3/-3.1	4075/46027	4246/45125	0.88 (0.79-0.96)	-		-14 (-26, -5)	67 (39, 198)
	Very very high	16	24.4	-8.6/-4.4	2361/13951	2340/12930	0.88 (0.77-1.02)	-		-25 (-54, +4)	40 (18, -204)

Thomopoulos C, Parati G, Zanchetti A: J Hyp 2014, 32 :2305

Effects of BP lowering in trails with average baseline BP in grade 1 and average low-to-moderate CV risk

	Trials	Baseline SBP/DBP	Difference SBP/DBP	Er (njp	vents atients)	RR	Standardized RR	Standardized RR	Absolute risk reduction 1000 pts/5 years	NNT 5 years
Outcome	(n)	(mmHg)	(mmHg)	Treated	Controls	(95% CI)	(95% CI)	(95% CI)	(95%CI)	(95% CI)
Stroke	4	146/91	-7.1/-4.5	71/4061	110/4012	0.58 (0.34-0.99)	0.33 (0.11–0.98)	b aragae an was	-21 (-26, -1)	47 (39, 1301)
CHD	5	145/91	-6.5/-4.2	114/4729	129/4246	0.75 (0.58-0.96)	0.68 (0.48-0.95)	ntos dite <u>sta</u> nt :	-12 (-18, -2)	86 (55, 531)
Stroke + CHD	4	146/91	-7.1/-4.5	159/4061	227/4012	0.69 (0.57–0.85)	0.51 (0.36-0.75)	nono <u>per</u> elation	-34 (-43, -19)	29 (23, 54)
CV death	4	146/91	-7.1/-4.5	53/4061	74/4012	0.71 (0.50–1.01)	0.57 (0.32–1.02)		-9 (-14, +1)	110 (72, –2223)
All-cause death	4	146/91	-7.1/-4.5	90/4061	133/4012	0.67 (0.51-0.87)	0.53 (0.35-0.80)	innen ter	-19 (-25, -8)	54 (40, 119)
								0.1 0.2 0.5 1 2	5	
								Active better Contro	ol better	

Zanchetti A: J Hyp 2014, 32 :2296-2304

Effects at different baseline and achieved blood pressure levels- overview and meta analysis of randomized trails

		now eluins h	i an	Difference	Eve (n/pa	ents tients)		- Himun'r	1. Spectra Large		Absolute risk reduction	NNT	
Outcome	Outcome	BP cut-off	Trials (n)	SBP/DBP (mmHg)	Treated	Controls	(95% CI)	Standardized RR (95% CI)	Standardized RR (95% CI)	P-value	1000 pts/5 years (95%CI)	5 years (95% CI)	P-value
a) sep	Stroke	140-149 vs 150-159 130-139 vs 140-149 120-129 vs 130-139	5 13 4	-12.6/-5.0 -7.0/-3.7 -6.3/-3.3	204/6562 1030/36655 259/12185	272/5844 1462/43081 340/12219	0.64 (0.53–0.76) 0.75 (0.65–0.85) 0.77 (0.66–0.90)	0.65 (0.54–0.77) 0.73 (0.63–0.83) 0.69 (0.55–0.86)		0.62	-19 (-24, -12) -11 (-15, -7) -9 (-14, -4)	52 (40, 78) 90 (67, 142) 106 (74, 231)	<0.001
	СНД	140–149 vs 150–159 130–139 vs 140–149 120–129 vs 130–139	5 14 5	-12.6/-5.0 -7.0/-3.7 -6.3/-3.5	194/6562 1089/37213 684/12853	173/5844 1395/43634 727/12453	0.78 (0.64–0.96) 0.82 (0.76–0.89) 0.92 (0.83–1.01)	0.79 (0.65–0.96) 0.77 (0.70–0.86) 0.88 (0.75–1.02)		0.12	-6 (-10, -1) -8 (-11, -5) -7 (-15, +1)	169 (100, 889) 122 (94, 198) 136 (67, -827)	0.37
	Stroke + CHD	140–149 vs 150–159 130–139 vs 140–149 120–129 vs 130–139	5 14 4	-12.6/-5.0 -7.0/-3.7 -6.3/-3.3	398/6562 2153/37559 917/12185	445/5844 2866/43381 1055/12219	0.70 (0.61-0.79) 0.79 (0.72-0.86) 0.87 (0.80-0.95)	0.71 (0.62–0.80) 0.73 (0.64–0.84) 0.81 (0.71–0.92)		0.24	-24 (-31, -16) -21 (-28, -13) -17 (-26, -7)	42 (32, 61) 47 (36, 76) 59 (39, 140)	0.26
	CV death	140–149 vs 150–159 130–139 vs 140–149 120–129 vs 130–139	5 14 5	-12.6/-5.0 -7.0/-3.7 -9.3/-4.5	291/6562 919/37559 325/12615	299/5844 1153/43381 377/12626	0.79 (0.68-0.93) 0.87 (0.77-0.99) 0.86 (0.74-1.00)	0.80 (0.70-0.93) 0.82 (0.69-0.98) 0.86 (0.74-1.00)		0.68	-13 (-19, -5) -6 (-9, -1) -5 (-9, 0)	77 (52, 215) 176 (103, 1040) 216 (117, ~)	0.097
	All-cause death	140–149 vs 150–159 130–139 vs 140–149 120–129 vs 130–139	5 14 5	-12.6/-5.0 -7.0/-3.7 -6.4/-3.4	583/6562 1699/37213 682/12615	570/5844 2051/43634 773/12626	0.86 (0.77-0.96) 0.92 (0.83-1.01) 0.88 (0.80-0.97)	0.87 (0.78–0.96) 0.89 (0.76–1.01) 0.81 (0.70–0.95)	*	0.29	-16 (-27, -5) -6 (-13, -1) -12 (-19, -3)	61 (37, 195) 164 (76, -1785) 83 (53, 315)	0.22
b) овр	Stroke	85–89 vs 90–94 75–79 vs 80–84	5 8	-11.0/-6.0 -5.6/-2.8	235/17362 1526/28405	405/17279 1781/27799	0.58 (0.50-0.68) 0.78 (0.68-0.89)	0.62 (0.55–0.72) 0.63 (0.49–0.81)	-	0.93	-9 (-11, -7) -32 (-42, -17)	110 (93, 149) 31 (24, 57)	<0.001
	СНО	85-89 vs 90-94 75-79 vs 80-84	4 10	-11.2/-6.0 -5.4/-2.4	698/16322 650/29631	831/16239 662/28586	0.85 (0.75-0.97) 0.90 (0.81-1.00)	0.87 (0.78-0.97) 0.78 (0.61-1.00)		0.30	-7 (-11, -2) -7 (-11, 0)	151 (89, 654) 149 (87, ∞)	0.99
	Stroke + CHD	85–89 vs 90–94 75–79 vs 80–84	4 8	-11.2/-6.0 -5.6/-2.8	896/16322 2146/28405	1157/16239 2435/27799	0.77 (0.71-0.84) 0.82 (0.73-0.92)	0.80 (0.75–0.86) 0.71 (0.58–0.87)	*	0.21	-14 (-18, -10) -38 (-52, -18)	69 (55, 99) 26 (19, 55)	0.014
	CV death	85–89 vs 90–94 75–79 vs 80–84	4 9	-11.2/-6.0 -5.6/-2.9	404/16322 945/28835	490/16239 992/28206	0.81 (0.69-0.96) 0.91 (0.83-0.99)	0.83 (0.72-0.97) 0.84 (0.70-0.98)		0.92	-5 (-8, -1) -8 (-15, -1)	196 (119, 1111) 123 (68, 948)	0.45
	All-cause death	85–89 vs 90–94 75–79 vs 80–84	5 11	-11.0/-6.0 -5.5/-2.9	805/17362 2162/29600	919/17279 2183/28961	0.88 (0.80-0.96) 0.95 (0.90-1.00)	0.89 (0.82-0.96) 0.90 (0.81-1.00)		0.86	-6 (-10, -2) -11 (-21, 0)	171 (105, 472) 88 (48, ∞)	0.25
		75–79 vs 80–84	11	-5.5/-2	.9	.9 2162/29600	.9 2162/29600 2183/28961	.9 2162/29600 2183/28961 0.95 (0.90–1.00)	.9 2162/29600 2183/28961 0.95 (0.90–1.00) 0.90 (0.81–1.00)	.9 2162/29600 2183/28961 0.95 (0.90-1.00) 0.90 (0.81-1.00)	.9 2162/29600 2183/28961 0.95 (0.90-1.00) 0.90 (0.81-1.00)	.9 2162/29600 2183/28961 0.95 (0.90-1.00) 0.90 (0.81-1.00) -11 (-21, 0)	.9 2162/29600 2183/28961 0.95 (0.90-1.00) 0.90 (0.81-1.00)11 (-21, 0) 88 (48, ∞)

Active better Control better

Zanchetti A: J Hyp 2014, 32 :2296-2304



The cumulative event incidence of primary outcome (nonfatal myocardial infarction, nonfatal stroke, and all-cause mortality in 6400 patients with diabetes mellitus of the INVEST trial in whom systolic blood pressure (SBP) remained ≥140 mm Hg or was reduced to between 130 and 139 mm Hg and <130 mm Hg (left).



Mancia G, and Grassi G Hypertension. 2014;63:29-36

Patients with achieved diastolic pressure ≤ 60mmHg vs 81-90mmHg

- \simeq 10 years older
- Higher rate of previous MI (47% vs 29%)
- Higher rate of previous stroke (12% vs 6%)
- Higher rate of heart failure (22% vs 4%)
- Higher rate of diabetes (44% vs 26%)
- Higher rate of cancer (11% vs 2%)

Unadjusted (A) and adjusted (B) relation between achieved (average in-treatment) diastolic blood pressure and risk of primary outcome in hypertensive patients with coronary artery disease enrolled in the International Verapamil-Trandolapril Study.





Verdecchia P et al. Hypertension, 2014:63:37-40

Canadian Hypertension Education Program 2014

New Recommendation:

When decreasing SBP to target levels in patients with established CHD (especially if systolic hypertension is present) be cautious when the DBP is \leq 60mmHg because of concerns that myocardial ischaemia might be exacerbated.

Conclusions J Curve

There is a J-Curve at around 60 mmHg

The data suggest excess mortality and morbidity is going to occur in frail elderly and these individuals cannot benefit from risk reduction programmes

One should monitor diastolic pressure closely below 65mmHg

AHA/ACC/ASH Scientific Statement2015

3.3. Recommendations

- 1. <u>The <140/90-mmHg BP target is reasonable for the</u> secondary prevention of cardiovascular events in patients with hypertension and CAD (*Class IIa; Level of Evidence B*).
- 2. A lower target BP (<130/80 mm Hg) may be appropriate in some individuals with CAD, previous MI, stroke or transient ischemic attack, or CAD risk equivalents (carotid artery disease, PAD, abdominal aortic aneurysm) (*Class IIb; Level of Evidence B*).
- 3. In patients with an elevated DBP and CAD with evidence of myocardial ischemia, the BP should be lowered slowly, and caution is advised in inducing decreases in DBP to <60 mm Hg in any patient with diabetes mellitus or who is >60 years of age. In older hypertensive individuals with wide pulse pressures, lowering SBP may cause very low DBP values (<60 mm Hg). This should alert the clinician to assess carefully any untoward signs or symptoms, especially those resulting from myocardial ischemia (*Class IIa*; *Level of Evidence C*).



Breaking News on Hypertension September, 11, 2015 New York, NY

National Heart Lung and Blood Institute (NHLBI) released breakthrough findings on the National Institute of Health's (NIH) Systolic Blood Pressure Intervention Trial (SPRINT)

which demonstrates that intensive management of systolic blood pressure to less than 120 mm Hg significantly reduces the risk of cardiovascular disease and risk of death in a population of adults 50 years of age or over.

The NHLBI announced blood pressure intervention was ended early so that the results could be disseminated quickly. A paper will be published in the next few months.

A Randomized trails invasive vs standard BP control- SPIRIT Trail

Subgroup	Intensive Treatment	Standard Treatment	Hazard Ratio (95% CI)	P Value for Interaction
our Brouh	no. of patients with prim	ary outcome/total no. (%)		mentenon
Overall	243/4678 (5.2)	319/4683 (6.8)	0.75 (0.64-0.89)	
Previous CKD				0.36
No	135/3348 (4.0)	193/3367 (5.7)	0.70 (0.56-0.87)	
Yes	108/1330 (8.1)	126/1316 (9.6)	0.82 (0.63-1.07)	
Age				0.32
<75 yr	142/3361 (4.2)	175/3364 (5.2)	0.80 (0.64-1.00)	
≥75 yr	101/1317 (7.7)	144/1319 (10.9) -	0.67 (0.51-0.86)	
Sex			—	0.45
Female	77/1684 (4.6)	89/1648 (5.4)	0.84 (0.62–1.14)	
Male	166/2994 (5.5)	230/3035 (7.6)	0.72 (0.59-0.88)	
Race				0.83
Black	62/1454 (4.3)	85/1493 (5.7)	0.77 (0.55-1.06)	
Nonblack	181/3224 (5.6)	234/3190 (7.3)	0.74 (0.61-0.90)	
Previous cardiovascular disease				0.39
No	149/3738 (4.0)	208/3746 (5.6)	0.71 (0.57-0.88)	
Yes	94/940 (10.0)	111/937 (11.8)	0.83 (0.62-1.09)	
Systolic blood pressure				0.77
≤132 mm Hg	71/1583 (4.5)	98/1553 (6.3) -	0.70 (0.51-0.95)	
>132 to <145 mm Hg	77/1489 (5.2)	106/1549 (6.8)	0.77 (0.57-1.03)	
≥145 mm Hg	95/1606 (5.9)	115/1581 (7.3)	0.83 (0.63-1.09)	
-		0.50	0.75 1.00 1.20	

Intensive Treatment Better Standard Treatment Better

Visit-to-Visit Variability of BP and CHD, Stroke, HF and Mortality-A cohort Study ALLHAT Post hoc Analysis



CHD = coronary heart disease; MI = myocardial infarction; SBP = systolic blood pressure.

Muntner P et all. Annals of internal Medicine 2015; 163: 329

Visit-to-Visit Variability of BP and CHD, Stroke, HF and Mortality-A cohort Study ALLHAT Post hoc Analysis

	Fatal CHD or Nonfatal MI	HR (95% CI)	All-Cause Mortality	HR (95% CI)
Aged <65 y -		1.15 (0.79–1.67)		1.67 (1.17–2.37)
Aged ≥65 y		1.34 (1.05–1.70)		1.49 (1.20–1.84)
Women		1.11 (0.77-1.61)	· · · · · · · · · · · · · · · · · · ·	1.47 (1.09–1.99)
Men		1.44 (1.11–1.86)		1.61 (1.31–1.99)
Black		1.47 (0.96-2.26)		1.40 (1.05–1.87)
Nonblack		1.25 (0.98-1.60)	and the second second	1.68 (1.34-2.10)
Diabetic		1.28 (0.91-1.82)		1.30 (0.96–1.74)
Nondiabetic		1.27 (0.97-1.67)	and the same second second	1.76 (1.40-2.20)
High adherence		1.21 (0.96-1.53)		1.50 (1.25–1.81)
Low adherence		2.11 (1.05-4.22)		2.01 (1.23-3.27)
Uncontrolled BP		1.40 (0.94-2.09)		1.79 (1.28-2.51)
Controlled BP		1.47 (1.12-1.93)	the burble into the second of the south	1.64 (1.30-2.06)
With LVH		1.67 (0.89-3.13)		1.04 (0.71–1.54)
Without LVH		1.22 (0.98-1.53)	Report of the second and find the	1.73 (1.41-2.12)
With a history of CVD		1.26 (0.94–1.69)		1.69 (1.32-2.17)
Without a history of CVD		1.27 (0.94–1.70)		1.37 (1.06–1.76)
Chlorthalidone		1.19 (0.88–1.61)		1.70 (1.34-2.17)
Amlodipine		1.52 (1.03-2.25)		1.43 (1.02–1.99)
Lisinopril —		1.09 (0.71–1.66)		1.57 (1.07-2.29)
	1	7		10
0.75	1.0 2.0	4.0	0.75 1.0 2.0	4.0
	HR		HR	

Muntner P et all. Annals of internal Medicine 2015; 163: 329







Journal of Hypertension: July 2015 - Volume 33 - Issue 7 - p 1321-1341 doi: 10.1097/HJH.0000000000000614 Reviews

Effects of blood pressure-lowering on outcome incidence in hypertension: 5. Head-to-head comparisons of various classes of antihypertensive drugs – overview and meta-analyses

Thomopoulos, Costas^a; Parati, Gianfranco^b; Zanchetti, Alberto^c

Abstract

Background and objectives: We have recently published an overview and meta-analysis of the effects of the five major classes of blood pressure-lowering drugs on cardiovascular outcomes when compared with placebo. However, possible differences in effectiveness of the various classes can correctly be estimated only by head-to-head comparisons of different classes of agents. This has been the objective of a new survey and meta-analysis.

Methods: A database search between 1966 and August 2014 ide ntified 50 eligible randomized controlled trials for 58 two-drug comparisons (247 006 patients for 1 029 768 patient-years). Risk ratios and their 95% confidence intervals of seven outcomes were estimated by a random-effects model.

Results: The effects of all drug classes are not significantly different on most outcomes when their blood pressure effect is equivalent. However, there are also significant differences involving almost all classes of drugs. When compared to all other classes together, diuretics are superior in preventing heart failure; beta-blockers less effective in preventing stroke; calcium antagonists superior in preventing stroke and all-cause death, but inferior in preventing heart failure; angiotensin-converting enzyme inhibitors more effective in preventing coronary heart disease and less in preventing stroke; angiotensin receptor blockers inferior in preventing coronary heart failure. When stratifying randomized controlled trials according to total cardiovascular risk, no drug class was found to change in effectiveness with the level of risk.

Conclusions: The results of all available evidence from head-to-head drug class comparisons do not allow the formulation of a fixed paradigm of drug choice valuable for all hypertensive patients, but the differences found may suggest specific choices in specific conditions, or preferable combinations of drugs.



Possible combinations of antihypertensive drug classes



Only dihydropyridines to be combined with β -blockers (except for verapamil or diltiazem for rate control in AF) Thiazides + β -blockers increase risk of new onset DM

ACEI + ARB combination discouraged (IIIA)

Percentage of Patients Reaching a Target SBP of Less than 140 mmHg with Different Classes of Antihypertensive Agents



Morgan et al., J Hypertens 2001; 14: 241-247

ALLHAT: Results

No significant difference was observed between amlodipine and the diuretic or lisinopril and the diuretic in the primary end point



1. ALLHAT Officers. JAMA 2002;288:(23):2981-2997.

BP Reduction and CV Events in LIFE



Dahlöf B et al Lancet 2002; 359: 995-1003

This calls for earlier intervention in the natural history of hypertension, before organ damage develops or when early damage can still be prevented.

The earlier the better



Treatment strategies in special conditions

- White Coat Hypertension
- Masked Hypertension
- Elderly
- Young Adults
- Women
- Diabetes Mellitus
- Metabolic Syndrome
- Obstructive Sleep Apnoea
- Diabetic / Non-diabetic
 Nephropathy
- Cerebrovascular Disease

- Heart Disease
- Atherosclerosis / Arteriosclerosis / Peripheral Artery Disease
- Sexual Dysfunction
- Resistant Hypertension
- Malignant Hypertension
- Hypertensive Emergencies / Urgencies
- Perioperative Management of Hypertension
- Renovascular Hypertension
- Primary Aldosteronism

Perioperative management of hypertension: Therapy CV Risk at the Peri-operative Period The Size of the Problem in the Europe

7 million major surgical procedures annually with MI rate 2 3% and CV mortality 0.5-1.5%

More than 150.000 patients suffered from major cardiac complication

✓ In the age group 75+, 12% of the women and 18% of the men have some degree of CVD

✓ By the year 2020, the elderly population will be increased by >50% and the annually conducted procedures by 25% CV Risk at the Peri-Operative Period The Size of the Problem

 Hypertension is a leading cause of death and disability in most Western societies

 Hypertension is the most frequent preoperative abnormality in surgical patients, with an overall prevalence of 20–25%.

 Preexisting hypertension is the most common medical reason for postponing surgery.
 Dix, P, Howell, Br J Anaesth 2001; 86:789.

Peri-Operative Hypertension

Hypertension occuring in the pre-operative, intraoperative or post-operative period.

Importance:

- Increased risk of cardiovascular events
- ✓ Increased post-operative morbidity and mortality
- ✓ Association with end-organ damage

Effects of Peri-Operative Hypertension

CVS effects:

✓ Increased BP→ \uparrow afterload & myocardial oxygen demand → myocardial oxygen supply and demand imbalance.

✓ Chronic \uparrow BP → myocardial hypertrophy → myocardial oxygen supply and demand imbalance

✓ Hypertrophied myocardium \rightarrow decreased compliance \rightarrow abnormal diastolic filling

Surgical Risk for Cardiac Events: Pathophysiology



Revised Cardiac Risk Index

Six Major Predictors:

- **1.** Ischemic Heart Disease
- 2. Cerebrovascular Disease
- 3. Heart Failure
- 4. Insulin Depended Diabetes Mellitus
- 5. Impaired Renal Function
- 6. High Risk Surgery

Each predictor
 contributes equally 1
 point

Score	Risk
0	0.4%
1	0.9%
2	7%
>3	11%

Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, Sugarbaker DJ, Donaldson MC, Poss R, Ho KK, Ludwig LE, Pedan A, Goldman L. Derivation and prospective validation of a simple index for predictionof cardiac risk of major noncardiac surgery. Circulation 1999;100:1043–1049.

BP Response During Anesthesia

- During the induction of anesthesia, sympathetic activation can cause the BP to rise by 20 - 30 mmHg and the HR to increase by 15 - 20 bpm in normotensive individuals.
 These responses may be more pronounced in patients with untreated hypertension
- As the period of anesthesia progresses, patients with preexisting hypertension are more likely to experience intraoperative BP lability (either hypotension or hypertension), which may lead to myocardial ischemia
- During the immediate postoperative period as patients recover from the effects of anesthesia, BP and HR slowly increase
- There is no evidence of superiority of any specific anaesthetic agent in noncardiac surgery

Wolfsthal, SD Med Clin North Am 1993; 77:349.

Treatment Algorithm Of Perioperative Hypertension



Preoperative β blockers

✓ Controversial

✓ Proven to be beneficial in cardiac surgeries
 ✓ For non-cardiac surgeries good results in high-risk
 patients but not in low-risk patients (NEJM 1996, 2005)

Associated with lesser incidences of perioperative ischemia
 Intraoperative hypotension, precipitation of asthamatic attack, major disadvantage

POISE Trial

✓ The biggest randomized controlled trial (N=8351)

✓ Patients with known CVD or >3 risk factors or major vascular surgery

✓ 100 mg metoprolol 2h prior operation
 ✓ 100 mg metoprolol 6h after operation
 ✓ 100 mg metoprolol maintenance dose 12h later

30% decrease in non-fatal MI

>33% increase in total mortality

2 fold increase in strokes

Probably due to Metoprolol Induced Hypotension and Iow HR

Risk Reduction using B-blockers

Lee index >3		Significant decrease in mortality
Lee index = 1 or 2	→ Nc	o significant difference
Lee index = 0		Increase in mortality

Preoperative b-blocker withdrawal

Increase in mortality

Association of b-blocker Therapy with Risks of Adverse CV Events and Deaths in Patients with Ischemic Heart Disease Undergoing Noncardiac Surgery: Danish Cohort Study

28.263 pts with CHD, non cardiac surgery

Table 2. Crude Numbers of Events

_	No. (%)							
	Heart	Failure	No Heart Failure					
Characteristic	β-Blockers (n = 4262)	No β-Blockers (n = 3728)	β-Blockers (n = 7419)	No <mark>β-Blockers</mark> (n = 12 854)				
30-d MACE	361 (8.0)	434 (12.0)	216 (3.0)	363 (3.0)				
Nonfatal stroke	1 (0.02)	5 (0.1)	13 (0.2)	29 (0.2)				
Nonfatal MI	67 (1.6)	57 (1.5)	57 (0.8)	121 (0.9)				
Cardiovascular death	293 (7.0)	372 (10.0)	146 (2.0)	213 (2.0)				
30-d All-cause mortality	427 (10.0)	558 (15.0)	279 (4.0)	509 (4.0)				

Andersson C et al. JAMA Intern Med 2014;174:336

Association of b-blocker Therapy with Risks of Adverse CV Events and Deaths in Patients with Ischemic Heart Disease Undergoing Noncardiac Surgery



The effects associated with β -blockers differed in patients with and without heart failure (HF) (P < .001 for interactions between β -blockers and HF for both end points). Among the subgroup without HF, the hazard ratios associated with β -blockers were further dependent on a history of MI and time elapsed since the most recent MI (for interaction between β -blockers and MI categories,

P < .001 for MACE and P = .02 for all-cause mortality). Analysis was adjusted for all variables from Table 1 plus calendar year for surgery. MACE indicates major adverse cardiovascular events (nonfatal ischemic stroke, acute myocardial infarction, and cardiovascular death); MI, myocardial infarction.

Andersson C et al. JAMA Intern Med 2014;174:336

Association of Perioperative b-blockade with Mortality and CV Morbidity Following Major Noncardiac Surgery



...perioperative b-blocker exposure was associated with lower rates of 30-day all-cause mortality in patients with 2 or more Revised Cardiac Risk Index factors

London MJ et al. JAMA 2013;309:1704

Recommendations on ACE inhibitor use

For a hypertensive patient already receiving ACE

inhibitors they should be discontinued 24 hours before

surgery and resume after patient's endovascular volume

has been stabilized. When they are prescribed for heart

failure their discontinuation at the preoperative phase

should be examined more carefully

Effects of Discontinuation of AllA Before Surgery on Hemodynamic Events In Hypertensive Patients Crhonically Treated With AllA

	Group I (AllA withdrawn)	Group II (AllA given)	р	
Systolic blood pressure				
Preinduction	159 ± 24	151 ± 26	NS	
Postinduction	126 ± 33	109 ± 24	NS	
Intubation	136 ± 34	121 ± 33	NS	
Lowesr value	159 ± 24	151 ± 26	NS	
Episodes of hypotension (No.)	1 ± 1	2 ± 1	<0.01	
Patients with at least 1 episode (No.)	12	19	<0.01	
Duration of episodes (min)	3 ± 4	8 ± 7	<0.01	
Patients receiving ephedrine (No.)	12	17	NS	
Dose of ephedrine (mg)	10 ± 10	15 ± 9	NS	
Patients receiving	0 Bertrand	5 M et Al., Anesth And	<0.02 Ilg 2001;92:	:26-3(

 <u>CONTINUE</u> antihypertensive medications in patients undergoing scheduled non-cardiac surgery *until the day of surgery*

 <u>CONTINUE</u> β-blockers and centrally acting antihypertensive drugs, otherwise rebound phenomena, including increase in BP and HR.

STOP in patients with preserved LVEF ACE inhibitors 24 hours before surgery, at least, and <u>RESTART</u> as soon as possible after hemodynamic and volume stabilization.

Recommendations On Calcium Channel Blockers

Recommendations	Clas s ^a	Level
It is recommended that calcium channel blockers be continued during non-cardiac surgery in patients with Prinzmetal angina pectoris	J	С
Heart rate-reducing calcium channel blockers, in particular diltiazem, may be considered before non-cardiac surgery in patients who have contra-indications to β -blockers	llb	С
Routine use of calcium channel blockers to reduce the risk of perioperative cardiovascular complications is not recommended		С
^a Class of recommendation		

^bLevel of evidence

Perioperative hypertension: parenteral drugs

SUSTAINED SBP ≥180 mmHg and/or DBP ≥110 mmHg Hypertensive Emergency Hypertensive Urgency

IMMEDIATE BP REDUCTION to minimize the ongoing target organ damage May require monitoring in an intensive care unit and parenteral drugs. REDUCE BP GRADUALLY <160/100 mm Hg *AVOID aggressive BP reductions:* may cause organ hypoperfusion. Parenteral drugs in case of emergent or urgent surgery

Agent (Dose)	Onset of action	Half- life	Duratio n of action	Mechanism of action	Preferred hypertensiv e condition
Enaprilat (0.5-5 mg bolus)	15 min.	35-38 h	4-6 h	Angiotensin- converting enzyme inhibitor	-Replacement of oral ACE inhibition in the perioperative setting -Congestive heart failure

Nicardipine (5-10 μg/Kg/min bolus) (1-3 μg/Kg/min infusion)	15 min.	45 min.	1-4 hours	Dihydropyridine type calcium antagonist Direct arterial vasodilator Increase in stroke volume and coronary blood flow Anti-ischemic properties	-Coronary artery disease -Heart failure -Acute renal failure -Acute
Clevidipine (2mg/h titrated by doubling the dose every 3 min. to maximum of 32 mg/h)	2-4 min.	2 min.	5-15 min		disease

Metoprolol	5 min.	3 - 7h	15 - 19h	Beta-1 selective	-Replacement of
(5mg boluses				blocker	oral beta-blocker
every 2-5 min					in the
up to 15 mg					perioperative
over 15 min)					setting
					-Beta blocker
					withdrawal
					-Tachycardia
				D . 1 .!	
Esmolol	1-2	2-10	10-20	Beta-1 selective	-Tachycardia
(infusion, 50-	min.	min.	min.	blocker	-Beta blocker
250					withdrawal
µg/Kg/min)					-Aortic dissection

Labetalol (bolus 2-10 mg, infusion 2.5-30 μg/Kg/min)	5-10 min.	5.5 hours	3-6 hours	Non selective beta blocker with alpha-1 blocking (at higher dose)	-Peripartum hypertension -Cardiac or cerebral ischemia -Aortic dissection -Pheochromocytoma
Phentolamine (1-4 mg boluses)	1-2 min.	20min	15-30min	Non selective alpha-blocker	-Pheochromocytoma (catecholamine excess)

Nitroglycerin	5	3	<3-5	Strong venodilator	-Acute
(infusion 20-200	min.	min.	min.	with mild	myocardial
μg/min, titration				peripheral arterial	ischemia
against BP)				dilation	-Established
				-Coronary artery	coronary artery
				vasodilation	disease
				-Reduction of left	-Acute
				ventricular preload	pulmonary
				-Reduction of	edema
				oxygen demand	

Sodium nitroprusside (infusion 0.3-2 µg/Kg/min)	Imme diate	2 min	1-2 min	Arterial and venous vasodilation	-Failure of other agents -Urgent reduction of severe acute hypertension
Urapidil (12.5-25 mg bolus followed by infusion of 5- 40mg/h)	3-5 min	2.7 h	4-6 h	Alpha blocker and central serotonin agonist activity	-Pheochromocytoma -Pre-eclampsia

Perioperative Management of HTN: Key Issues-1

- Some surgical procedure are associated with a high incidence of HTN: carotid endoarteriectomy, head and neck surgery, aortic and peripheral vascular surgery
- ✓ BP levels > 180/110 mmHg should be controlled prior to surgery; for elective surgery (cardiac, vascular), effective BP control can be achieved over several days to weeks of outpatient treatment
- Uncontrolled HTN before surgery is associated with wider fluctuations of BP during induction of anesthesia and intubation and may increase the risk for perioperative ischemic events
- Surgical candidates with controlled HTN should mantain their medications until the time of surgery (except for ACEI and ARB's), and therapy should be re-instituted as soon as possible postoperatively

Mod. from JNC VII

Perioperative Management Of HTN: Key Issues-2

- ✓ If a patients develops intraoperative HTN, it is necessary ascertain that other causes of HTN have been ruled out (hypercapnia, distend bladder, hypertemia, hypoxia)
- In urgent situations, rapidly acting parenteral agents can be utilized to achieve BP control very rapidly
- ✓ Sudden intraoperative HTN is managed by the same parenteal antihypertensive agents that are utilized in the management of hypertensive emergencies
- ✓ HTN is very common in the early postoperative period and is related to increased sympathetic tone and vascular resistance that follows pain and increased intravascular volume, and may require parenteral drug and/ or (if possible) the re-insitution of previous oral treatment.

Mod. from JNC VII