



Hipertansiyonda Yenilikler

Prof. Dr. Tevfik Ecdar

Demirođlu Bilim Üniversitesi Tıp Fakóltesi

İç Hastalıkları Anabilim Dalı

Nefroloji Bilim Dalı

Çalışmalar, Kılavuzlar ve Hipertansiyon Tanımları

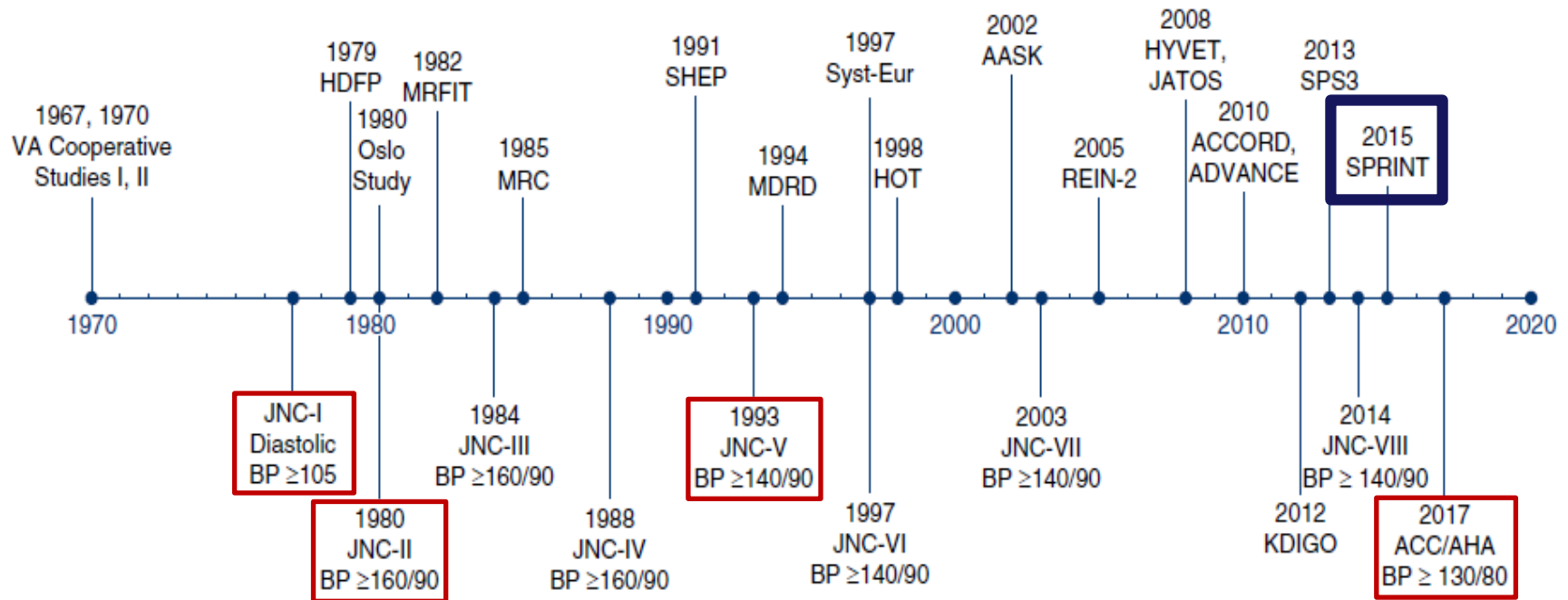


Figure 1. | The Definition of Hypertension per United States BP Guidelines has Changed Over Time. Above timeline: major hypertension trials from 1960 to 2018 (6,34–37,39,55–66). Below timeline: guideline and definition of hypertension, from 1960 to 2018 (3–5,9–11,14,67–69). ADVANCE, The Action in Diabetes and Vascular Disease: Preterax and Diamicron Controlled Evaluation trial; ALLHAT, The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; HDFP, The Hypertension Detection and Follow-up Program; HOT, The Hypertension Optimal Treatment study; HTN, Hypertension; HYVET, The Hypertension in the Very Elderly Trial; JATOS, The Japanese Trial to Assess Optimal Systolic BP in Elderly Hypertensive Patients; KDIGO, Kidney Disease Improving Global Outcomes; MRC, Medical Research Council; MRFIT, Multiple Risk Factor Intervention Trial; SHEP, The Systolic Hypertension in the Elderly Program; SPS3, The Secondary Prevention of Small Subcortical Strokes trial; Syst-Eur, The Systolic Hypertension in Europe trial; UKPDS, The United Kingdom Prospective Diabetes Study; VA, Veterans Affairs.

SPRINT

(Systolic Blood Pressure Intervention Trial)



A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*

ABSTRACT

BACKGROUND

The most appropriate targets for systolic blood pressure to reduce cardiovascular morbidity and mortality among persons without diabetes remain uncertain.

METHODS

We randomly assigned 9361 persons with a systolic blood pressure of 130 mm Hg or higher and an increased cardiovascular risk, but without diabetes, to a systolic blood-pressure target of less than 120 mm Hg (intensive treatment) or a target of less than 140 mm Hg (standard treatment). The primary composite outcome was myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from cardiovascular causes.

RESULTS

At 1 year, the mean systolic blood pressure was 121.4 mm Hg in the intensive-treatment group and 136.2 mm Hg in the standard-treatment group. The intervention was stopped early after a median follow-up of 3.26 years owing to a significantly lower rate of the primary composite outcome in the intensive-treatment group than in the standard-treatment group (1.65% per year vs. 2.19% per year; hazard ratio with intensive treatment, 0.75; 95% confidence interval [CI], 0.64 to 0.89; $P < 0.001$). All-cause mortality was also significantly lower in the intensive-treatment group (hazard ratio, 0.73; 95% CI, 0.60 to 0.90; $P = 0.003$). Rates of serious adverse events of hypotension, syncope, electrolyte abnormalities, and acute kidney injury or failure, but not of injurious falls, were higher in the intensive-treatment group than in the standard-treatment group.

CONCLUSIONS

Among patients at high risk for cardiovascular events but without diabetes, targeting a systolic blood pressure of less than 120 mm Hg, as compared with less than 140 mm Hg, resulted in lower rates of fatal and nonfatal major cardiovascular events and death from any cause, although significantly higher rates of some adverse events were observed in the intensive-treatment group. (Funded by the National Institutes of Health; ClinicalTrials.gov number, NCT01206062.)

The members of the writing committee (Jackson T. Wright, Jr., M.D., Ph.D., Jeff D. Williamson, M.D., M.H.S., Paul K. Whelton, M.D., Joni K. Snyder, R.N., B.S.N., M.A., Kaycee M. Sink, M.D., M.A.S., Michael V. Rocco, M.D., M.S.C.E., David M. Reboussin, Ph.D., Mahboob Rahman, M.D., Suzanne Oparil, M.D., Cora E. Lewis, M.D., M.S.P.H., Paul L. Kimmel, M.D., Karen C. Johnson, M.D., M.P.H., David C. Goff, Jr., M.D., Ph.D., Lawrence J. Fine, M.D., Dr.P.H., Jeffrey A. Cutler, M.D., M.P.H., William C.ushman, M.D., Alfred K. Cheung, M.D., and Walter T. Ambrosius, Ph.D.) assume responsibility for the overall content and integrity of the article. The affiliations of the members of the writing group are listed in the Appendix. Address reprint requests to Dr. Wright at the Division of Nephrology and Hypertension, University Hospitals Case Medical Center, Case Western Reserve University, 1100 Euclid Ave. Cleveland, OH 44106-6053, or at jackson.wright@case.edu.

*A complete list of the members of the Systolic Blood Pressure Intervention Trial (SPRINT) Research Group is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on November 9, 2015, at NEJM.org.

N Engl J Med 2015;373:2103-16.

DOI: 10.1056/NEJMoa1511939

Copyright © 2015 Massachusetts Medical Society.

- Çok merkezli, randomize, kontrollü, açık etiketli çalışma
- Amerika Birleşik Devletleri'ndeki 102 merkez
- Sistolik kan basıncı (SKB) ≥ 130 mm Hg olan, yüksek kardiyovasküler riski olan* fakat diyabeti olmayan 9361 hasta
- Hastalar yoğun tedavi (SKB < 120 mm Hg) veya standart tedavi (SKB < 130 mm Hg) gruplarına randomize edildiler.
- Birincil birleşik sonlanım noktası: Miyokard infarktüsü, diğer akut koroner sendromlar, inme, kalp yetersizliği veya KV nedenlere bağlı ölüm

**İnme dışında klinik veya subklinik KV hastalık; eGFR'nin 20 – 60 ml/dak/1.73 m² olduğu KBH (polikistik böbrek hastalığı dışında), Framingham risk skorlamasına göre 10 yıllık KV riskin \geq %15 olması; > 75 yaş*

SPRINT

(Systolic Blood Pressure Intervention Trial)

Table 1. Baseline Characteristics of the Study Participants.*

Characteristic	Intensive Treatment (N= 4678)	Standard Treatment (N= 4683)
Criterion for increased cardiovascular risk — no. (%) [†]		
Age ≥75 yr	1317 (28.2)	1319 (28.2)
Chronic kidney disease [‡]	1330 (28.4)	1316 (28.1)
Cardiovascular disease	940 (20.1)	937 (20.0)
Clinical	779 (16.7)	783 (16.7)
Subclinical	247 (5.3)	246 (5.3)
Framingham 10-yr cardiovascular disease risk score ≥15%	2870 (61.4)	2867 (61.2)
Female sex — no. (%)	1684 (36.0)	1648 (35.2)
Age — yr		
Overall	67.9±9.4	67.9±9.5
Among those ≥75 yr of age	79.8±3.9	79.9±4.1
Race or ethnic group — no. (%) [§]		
Non-Hispanic black	1379 (29.5)	1423 (30.4)
Hispanic	503 (10.8)	481 (10.3)
Non-Hispanic white	2698 (57.7)	2701 (57.7)
Other	98 (2.1)	78 (1.7)
Black race ^{§¶}	1454 (31.1)	1493 (31.9)

SPRINT

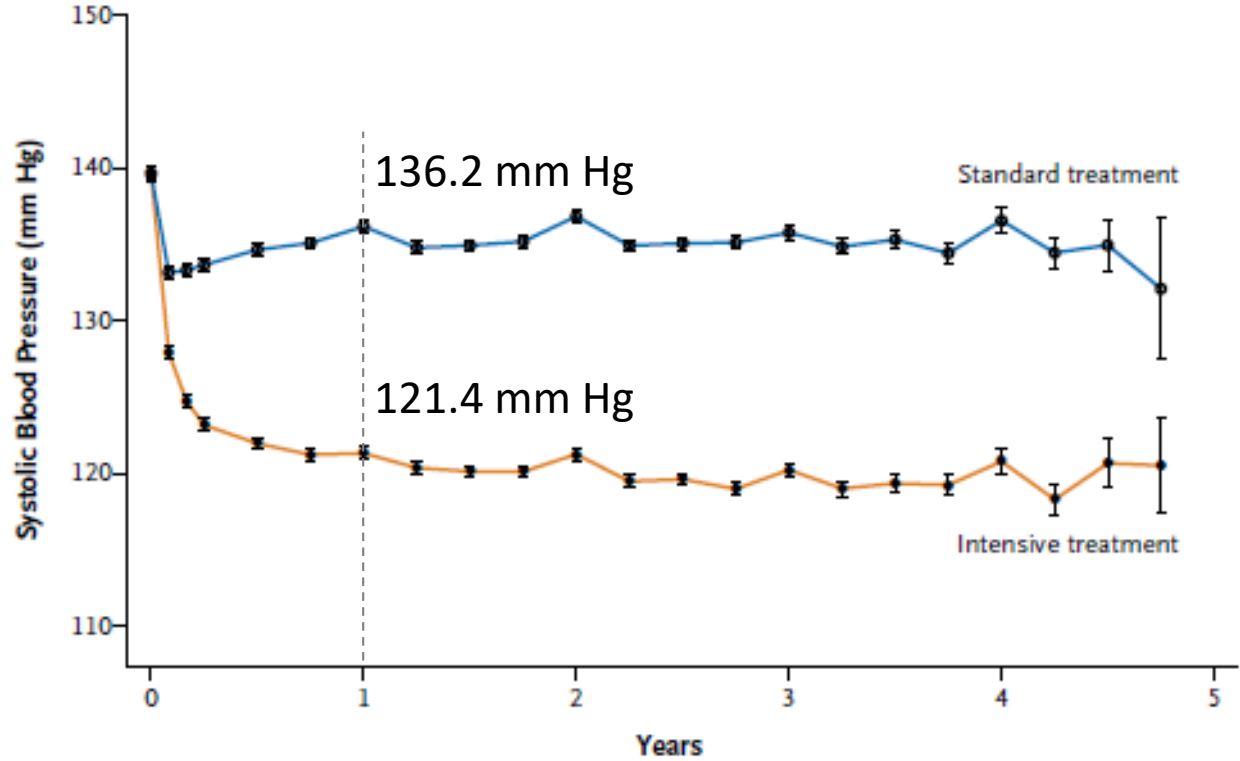
(Systolic Blood Pressure Intervention Trial)

Table 1. Baseline Characteristics of the Study Participants.*

Characteristic	Intensive Treatment (N= 4678)	Standard Treatment (N= 4683)
Baseline blood pressure — mm Hg		
Systolic	139.7±15.8	139.7±15.4
Diastolic	78.2±11.9	78.0±12.0
Distribution of systolic blood pressure — no. (%)		
≤132 mm Hg	1583 (33.8)	1553 (33.2)
>132 mm Hg to <145 mm Hg	1489 (31.8)	1549 (33.1)
≥145 mm Hg	1606 (34.3)	1581 (33.8)
Serum creatinine — mg/dl	1.07±0.34	1.08±0.34
Estimated GFR — ml/min/1.73 m ²		
Among all participants	71.8±20.7	71.7±20.5
Among those with estimated GFR ≥60 ml/min/1.73 m ²	81.3±15.5	81.1±15.5
Among those with estimated GFR <60 ml/min/1.73 m ²	47.8±9.5	47.9±9.5
Ratio of urinary albumin (mg) to creatinine (g)	44.1±178.7	41.1±152.9
Fasting total cholesterol — mg/dl	190.2±41.4	190.0±40.9
Fasting HDL cholesterol — mg/dl	52.9±14.3	52.8±14.6
Fasting total triglycerides — mg/dl	124.8±85.8	127.1±95.0
Fasting plasma glucose — mg/dl	98.8±13.7	98.8±13.4
Statin use — no./total no. (%)	1978/4645 (42.6)	2076/4640 (44.7)
Aspirin use — no./total no. (%)	2406/4661 (51.6)	2350/4666 (50.4)

SPRINT

(Systolic Blood Pressure Intervention Trial)



Çalışma medyan 3.26 yıllık bir takip sonrasında durduruldu!

SPRINT

(Systolic Blood Pressure Intervention Trial)

Outcome	Intensive Treatment		Standard Treatment		Hazard Ratio (95% CI)	P Value
	no. of patients (%)	% per year	no. of patients (%)	% per year		
All participants	(N = 4678)		(N = 4683)			
Primary outcome†	243 (5.2)	1.65	319 (6.8)	2.19	0.75 (0.64–0.89)	<0.001
Secondary outcomes						
Myocardial infarction	97 (2.1)	0.65	116 (2.5)	0.78	0.83 (0.64–1.09)	0.19
Acute coronary syndrome	40 (0.9)	0.27	40 (0.9)	0.27	1.00 (0.64–1.55)	0.99
Stroke	62 (1.3)	0.41	70 (1.5)	0.47	0.89 (0.63–1.25)	0.50
Heart failure	62 (1.3)	0.41	100 (2.1)	0.67	0.62 (0.45–0.84)	0.002
Death from cardiovascular causes	37 (0.8)	0.25	65 (1.4)	0.43	0.57 (0.38–0.85)	0.005
Death from any cause	155 (3.3)	1.03	210 (4.5)	1.40	0.73 (0.60–0.90)	0.003
Primary outcome or death	332 (7.1)	2.25	423 (9.0)	2.90	0.78 (0.67–0.90)	<0.001
Participants with CKD at baseline	(N = 1330)		(N = 1316)			
Composite renal outcome‡	14 (1.1)	0.33	15 (1.1)	0.36	0.89 (0.42–1.87)	0.76
≥50% reduction in estimated GFR§	10 (0.8)	0.23	11 (0.8)	0.26	0.87 (0.36–2.07)	0.75
Long-term dialysis	6 (0.5)	0.14	10 (0.8)	0.24	0.57 (0.19–1.54)	0.27
Kidney transplantation	0		0			
Incident albuminuria¶	49/526 (9.3)	3.02	59/500 (11.8)	3.90	0.72 (0.48–1.07)	0.11
Participants without CKD at baseline 	(N = 3332)		(N = 3345)			
≥30% reduction in estimated GFR to <60 ml/min/1.73 m ² §	127 (3.8)	1.21	37 (1.1)	0.35	3.49 (2.44–5.10)	<0.001
Incident albuminuria¶	110/1769 (6.2)	2.00	135/1831 (7.4)	2.41	0.81 (0.63–1.04)	0.10

Birincil Birleşik Sonlanım Noktası: Miyokard infarktüsü, diğer akut koroner sendromlar, inme, kalp yetersizliği veya kardiyovasküler nedenlere bağlı ölüm

SPRINT

(Systolic Blood Pressure Intervention Trial)

Variable	Intensive Treatment (N= 4678)	Standard Treatment (N= 4683)	Hazard Ratio	P Value
	<i>no. of patients (%)</i>			
Serious adverse event*	1793 (38.3)	1736 (37.1)	1.04	0.25
Conditions of interest				
Serious adverse event only				
Hypotension	110 (2.4)	66 (1.4)	1.67	0.001
Syncope	107 (2.3)	80 (1.7)	1.33	0.05
Bradycardia	87 (1.9)	73 (1.6)	1.19	0.28
Electrolyte abnormality	144 (3.1)	107 (2.3)	1.35	0.02
Injurious fall†	105 (2.2)	110 (2.3)	0.95	0.71
Acute kidney injury or acute renal failure‡	193 (4.1)	117 (2.5)	1.66	<0.001
Emergency department visit or serious adverse event				
Hypotension	158 (3.4)	93 (2.0)	1.70	<0.001
Syncope	163 (3.5)	113 (2.4)	1.44	0.003
Bradycardia	104 (2.2)	83 (1.8)	1.25	0.13
Electrolyte abnormality	177 (3.8)	129 (2.8)	1.38	0.006
Injurious fall†	334 (7.1)	332 (7.1)	1.00	0.97
Acute kidney injury or acute renal failure‡	204 (4.4)	120 (2.6)	1.71	<0.001
Monitored clinical events				
Adverse laboratory measure§				
Serum sodium <130 mmol/liter	180 (3.8)	100 (2.1)	1.76	<0.001
Serum sodium >150 mmol/liter	6 (0.1)	0		0.02
Serum potassium <3.0 mmol/liter	114 (2.4)	74 (1.6)	1.50	0.006
Serum potassium >5.5 mmol/liter	176 (3.8)	171 (3.7)	1.00	0.97
Orthostatic hypotension¶				
Alone	777 (16.6)	857 (18.3)	0.88	0.01
With dizziness	62 (1.3)	71 (1.5)	0.85	0.35

The unobserved measurements in SPRINT were no doubt intentional, both for the optimal standardization of measurements and for the quality of SPRINT, and in order to avoid the alert or white coat effect without depending on ambulatory BP measurements. However, the implications thereof are that BPs taken in SPRINT cannot be directly compared with BPs in other trials, and that the treatment arm < 120 mmHg in SPRINT compares with a higher SBP value close to 140 mmHg in other trials. Thus, the SBP target in the treatment of hypertension remains unchanged at < 140 mmHg.

The BP measurement technique is one of the many puzzling aspects of SPRINT. We have previously^{10,11} pointed out several other points of interest that must be taken into account when assessing the true nature of SPRINT and whether the results from SPRINT are useful in daily clinical work.

Whelton PK, et al.

2017 High Blood Pressure Clinical Practice Guideline

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on
Clinical Practice Guidelines

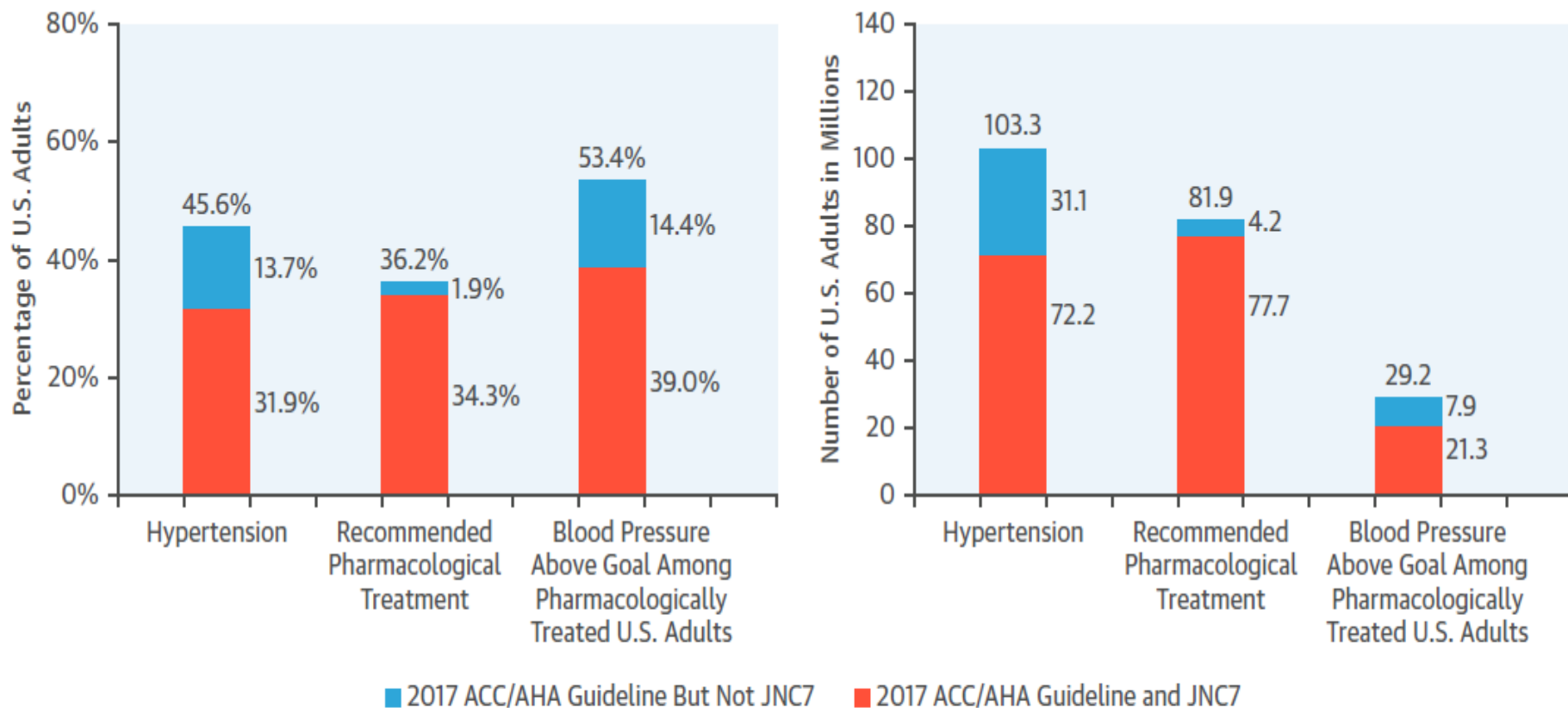
Table 6. Categories of BP in Adults*

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120–129 mm Hg	and	<80 mm Hg
Hypertension			
Stage 1	130–139 mm Hg	or	80–89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

*Individuals with SBP and DBP in 2 categories should be designated to the higher BP category.

BP indicates blood pressure (based on an average of ≥2 careful readings obtained on ≥2 occasions, as detailed in Section 4); DBP, diastolic blood pressure; and SBP systolic blood pressure.

2017 ACC/AHA Kılavuzu ve JNC7



Muntner, P. et al. *J Am Coll Cardiol.* 2018;71(2):109-18.

This graph shows the percentage (left) and number (right) of U.S. adults with hypertension, recommended pharmacological treatment, and with blood pressure above goal among those receiving pharmacological treatment according to the 2017 ACC/AHA guideline (full bar height), the JNC7 guideline (orange bars), and the 2017 ACC/AHA guideline but not the JNC7 guideline (blue bars). ACC/AHA = American College of Cardiology/American Heart Association; JNC7 = Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure.

Whelton PK, et al.

2017 High Blood Pressure Clinical Practice Guideline

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on
Clinical Practice Guidelines

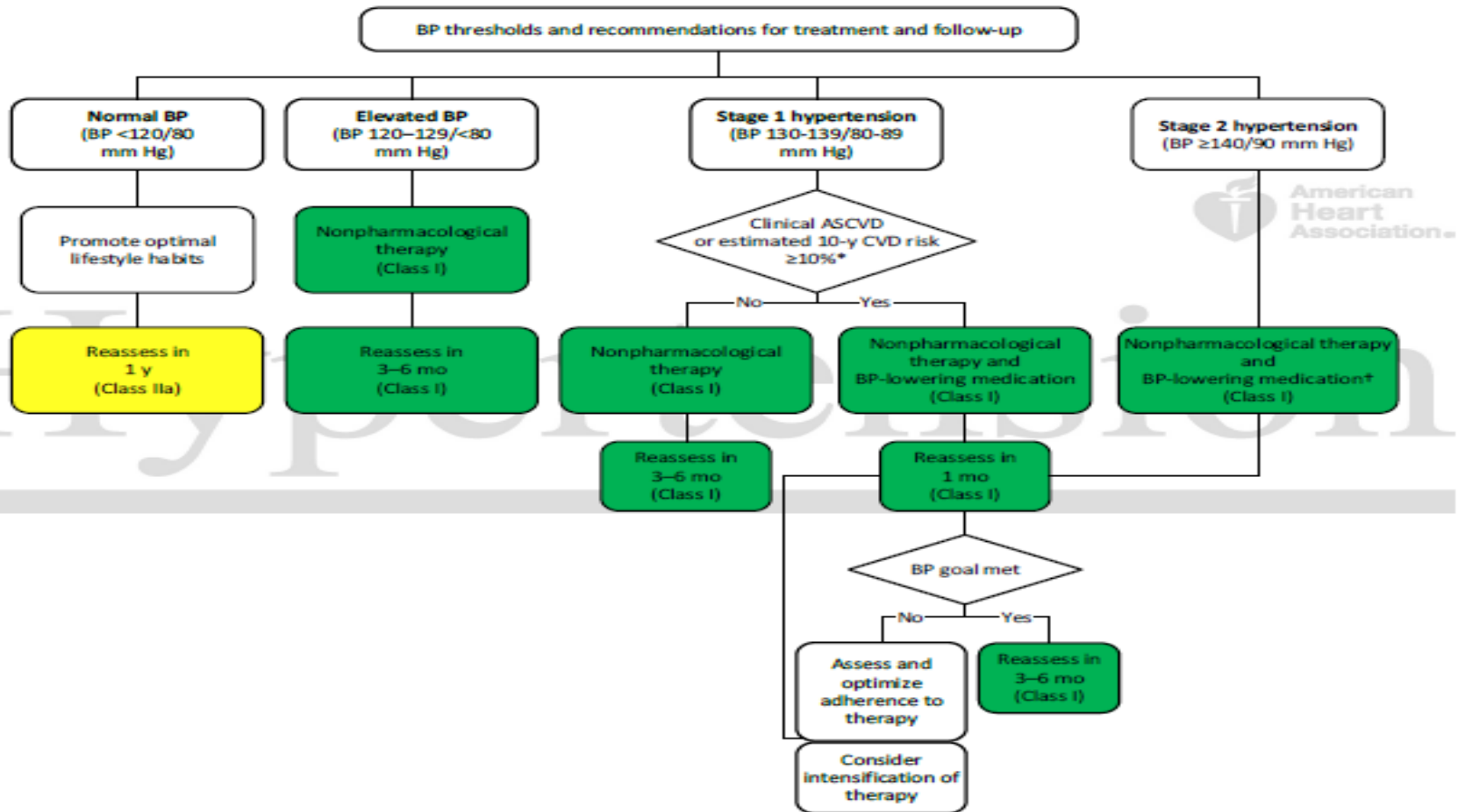
8.1.6. Choice of Initial Medication

Recommendation for Choice of Initial Medication		
References that support the recommendation are summarized in Online Data Supplement 27 and Systematic Review Report.		
COR	LOE	Recommendation
I	A ^{SR}	1. For initiation of antihypertensive drug therapy, <u>first-line agents include thiazide diuretics, CCBs, and ACE inhibitors or ARBs. (1, 2)</u>

SR indicates systematic review.



2017 ACC/AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults



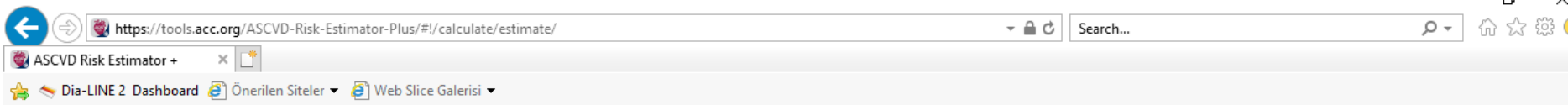
Colors correspond to Class of Recommendation in Table 1.

*Using the ACC/AHA Pooled Cohort Equations (57). Note that patients with DM or CKD are automatically placed in the high-risk category. For initiation of RAS inhibitor or diuretic therapy, assess blood tests for electrolytes and renal function 2 to 4 weeks after initiating therapy.

†Consider initiation of pharmacological therapy for stage 2 hypertension with 2 antihypertensive agents of different classes. Patients with stage 2 hypertension and BP ≥160/100 mm Hg should be promptly treated, carefully monitored, and subject to upward medication dose adjustment as necessary to control BP. Reassessment includes BP measurement, detection of orthostatic hypotension in selected patients (e.g., older or with postural symptoms), identification of white coat hypertension or a white coat effect, documentation of adherence, monitoring of the

ASCVD

(Atherosclerotic Cardiovascular Disease)



ASCVD Risk Estimator Plus

Estimate Risk

Therapy Impact

Advice

App is intended for primary prevention patients (without ASCVD).

Current Age ⓘ *

Age must be between 20-79

Sex *

Male	Female
------	--------

Race *

White	African American	Other
-------	------------------	-------

Systolic Blood Pressure (mm Hg) *

Value must be between 90-200

Diastolic Blood Pressure (mm Hg) ○

Value must be between 60-130

Total Cholesterol (mg/dL) *

Value must be between 130 - 320

HDL Cholesterol (mg/dL) *

Value must be between 20 - 100

LDL Cholesterol (mg/dL) ⓘ ○

Value must be between 30-300

History of Diabetes? *

Yes	No
-----	----

Smoker: ⓘ *

Yes	Former	No
-----	--------	----

On Hypertension Treatment? *

On a Statin? ⓘ ○

On Aspirin Therapy? ⓘ ○

2017 ACC/AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

Table 23. BP Thresholds for and Goals of Pharmacological Therapy in Patients With Hypertension According to Clinical Conditions

Clinical Condition(s)	BP Threshold, mm Hg	BP Goal, mm Hg
General		
Clinical CVD or 10-year ASCVD risk $\geq 10\%$	$\geq 130/80$	$< 130/80$
No clinical CVD and 10-year ASCVD risk $< 10\%$	$\geq 140/90$	$< 130/80$
Older persons (≥ 65 years of age; noninstitutionalized, ambulatory, community-living adults)	≥ 130 (SBP)	< 130 (SBP)
Specific comorbidities		
Diabetes mellitus	$\geq 130/80$	$< 130/80$
Chronic kidney disease	$\geq 130/80$	$< 130/80$
Chronic kidney disease after renal transplantation	$\geq 130/80$	$< 130/80$
Heart failure	$\geq 130/80$	$< 130/80$
Stable ischemic heart disease	$\geq 130/80$	$< 130/80$
Secondary stroke prevention	$\geq 140/90$	$< 130/80$
Secondary stroke prevention (lacunar)	$\geq 130/80$	$< 130/80$
Peripheral arterial disease	$\geq 130/80$	$< 130/80$

ASCVD indicates atherosclerotic cardiovascular disease; BP, blood pressure; CVD, cardiovascular disease; and SBP, systolic blood pressure.

2018 ESC/ESH Guidelines for the management of arterial hypertension

Table 3 Classification of office blood pressure^a and definitions of hypertension grade^b

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension ^b	≥140	and	<90

BP = blood pressure; SBP = systolic blood pressure.

^aBP category is defined according to seated clinic BP and by the highest level of BP, whether systolic or diastolic.

^bIsolated systolic hypertension is graded 1, 2, or 3 according to SBP values in the ranges indicated.

The same classification is used for all ages from 16 years.

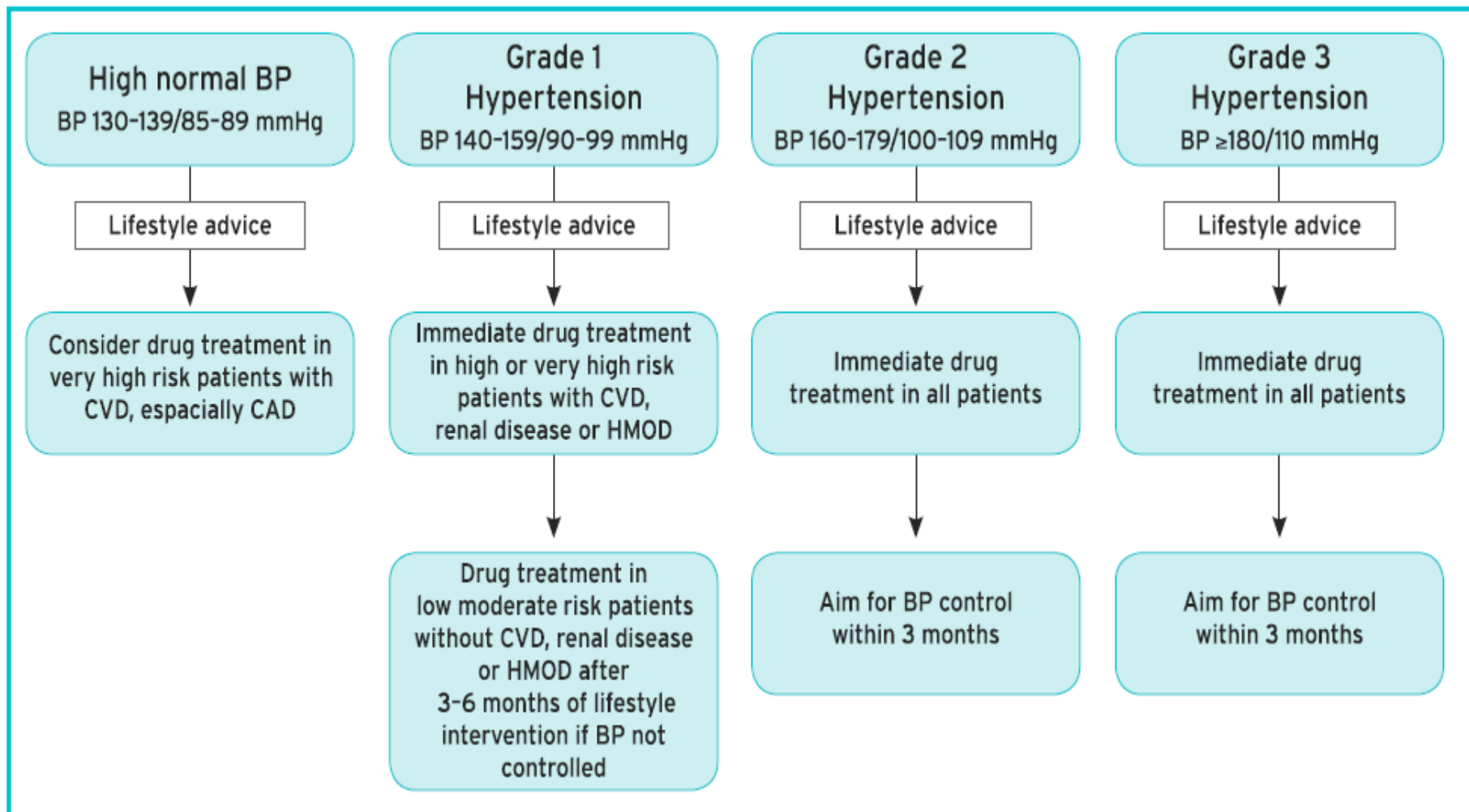
2018 ESC/ESH Guidelines for the management of arterial hypertension

Hypertension disease staging	Other risk factors, HMOD, or disease	BP (mmHg) grading			
		High normal SBP 130-139 DBP 85-89	Grade 1 SBP 140-159 DBP 90-99	Grade 2 SBP 160-179 DBP 100-109	Grade 3 SBP \geq 180 or DBP \geq 110
Stage 1 (uncomplicated)	No other risk factors	Low risk	Low risk	Moderate risk	High risk
	1 or 2 risk factors	Low risk	Moderate risk	Moderate to high risk	High risk
	\geq 3 risk factors	Low to Moderate risk	Moderate to high risk	High Risk	High risk
Stage 2 (asymptomatic disease)	HMOD, CKD grade 3, or diabetes mellitus without organ damage	Moderate to high risk	High risk	High risk	High to very high risk
Stage 3 (established disease)	Established CVD, CKD grade \geq 4, or diabetes mellitus with organ damage	Very high risk	Very high risk	Very high risk	Very high risk

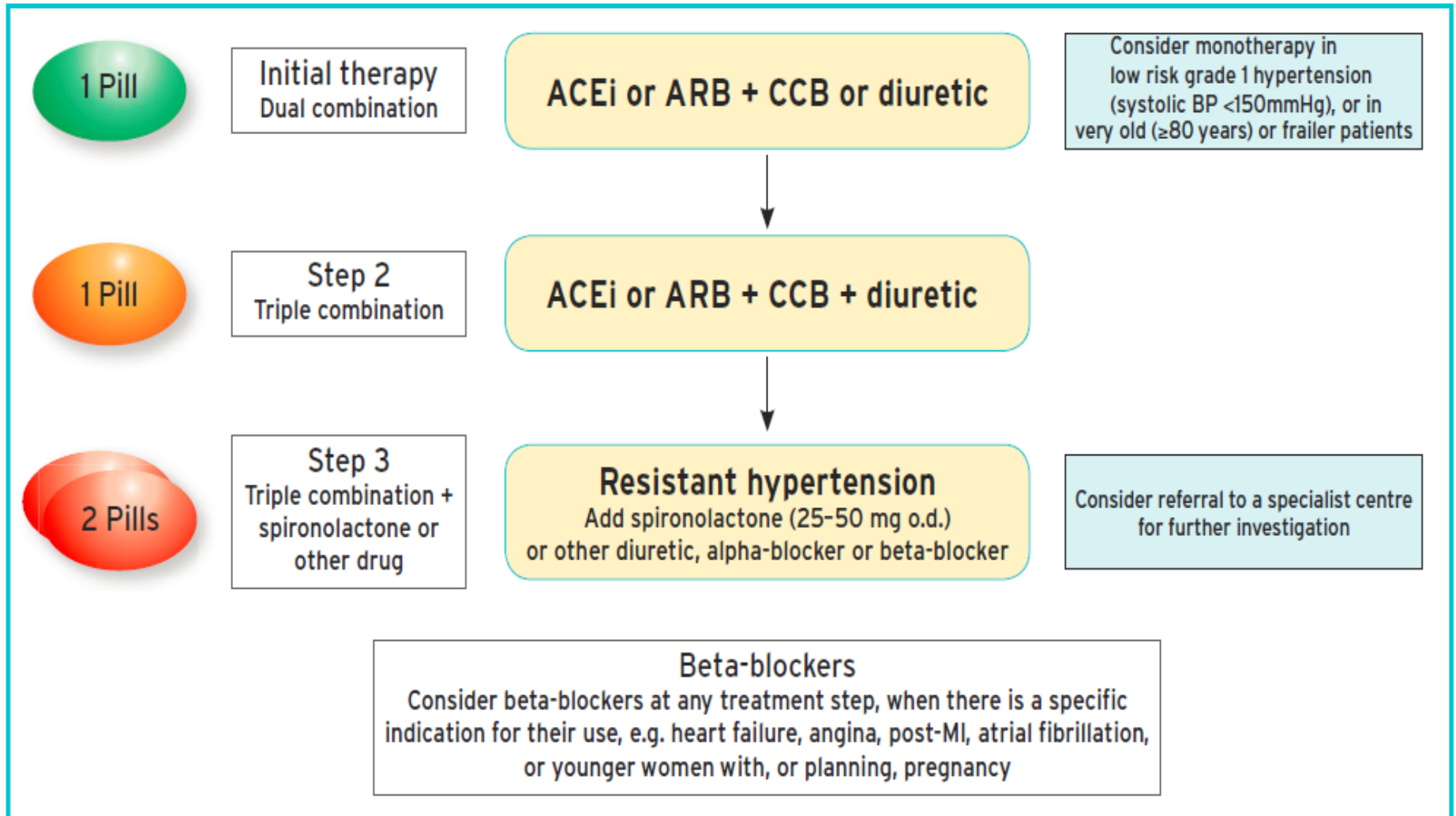
©ESC/ESH 2018

Figure 1 Classification of hypertension stages according to blood pressure levels, presence of cardiovascular risk factors, hypertension-mediated organ damage, or comorbidities. CV risk is illustrated for a middle-aged male. The CV risk does not necessarily correspond to the actual risk at different ages. The use of the SCORE system is recommended for formal estimation of CV risk for treatment decisions. BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; DBP = diastolic blood pressure; HMOD = hypertension-mediated organ damage; SBP = systolic blood pressure; SCORE = Systematic COronary Risk Evaluation.

2018 ESC/ESH Guidelines for the management of arterial hypertension



2018 ESC/ESH Guidelines for the management of arterial hypertension



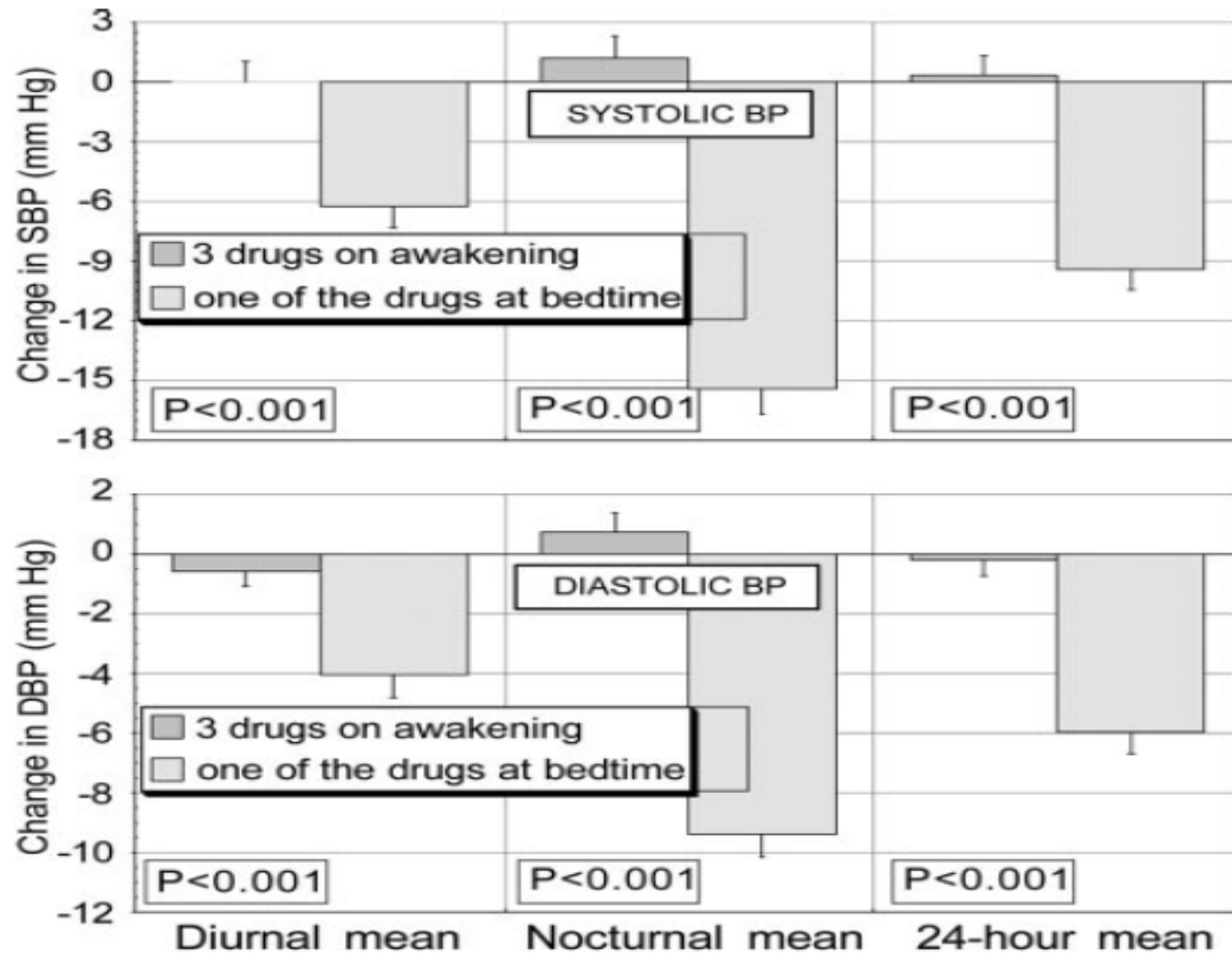
Chronotherapy in Resistant Hypertension

Chronotherapy Improves Blood Pressure Control and Reverts the Nondipper Pattern in Patients With Resistant Hypertension

Ramón C. Hermida, Diana E. Ayala, José R. Fernández, Carlos Calvo

Abstract—Therapeutic strategies in resistant hypertension include adding another drug or changing drugs in search for a better synergic combination. Most patients, however, receive all of their drugs in a single morning dose. We have evaluated the impact on the circadian pattern of blood pressure on modifying the time of treatment without increasing the number of prescribed drugs. We studied 250 hypertensive patients who were receiving 3 antihypertensive drugs in a single morning dose. Patients were randomly assigned to 1 of 2 groups according to the modification in their treatment strategy: changing 1 of the drugs but keeping all 3 in the morning or the same approach but administering the new drug at bedtime. Blood pressure was measured for 48 hours before and after 12 weeks of treatment. There was no effect on ambulatory blood pressure when all of the drugs were taken on awakening. The baseline prevalence of nondipping (79%) was slightly increased after treatment (86%; $P=0.131$). The ambulatory blood pressure reduction was statistically significant (9.4/6.0 mm Hg for systolic/diastolic blood pressure; $P<0.001$) with 1 drug at bedtime. This reduction was larger in the nocturnal than in the diurnal mean of blood pressure. Thus, whereas only 16% of the patients in this group were dippers at baseline, 57% were dippers after therapy ($P<0.001$). Results indicate that, in resistant hypertension, time of treatment may be more important for blood pressure control and for the proper modeling of the circadian blood pressure pattern than just changing the drug combination. (*Hypertension*. 2008;51:69-76.)

Chronotherapy Improves Blood Pressure Control and Reverts the Nondipper Pattern in Patients With Resistant Hypertension



Bedtime Dosing of Antihypertensive Medications Reduces Cardiovascular Risk in CKD

Ramón C. Hermida, Diana E. Ayala, Artemio Mojón, and José R. Fernández

Bioengineering and Chronobiology Laboratories, University of Vigo, Campus Universitario, Vigo, Spain

ABSTRACT

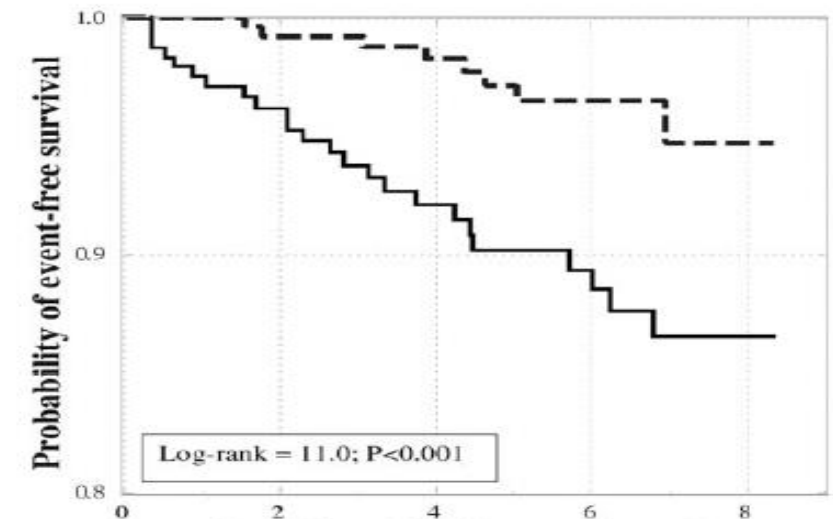
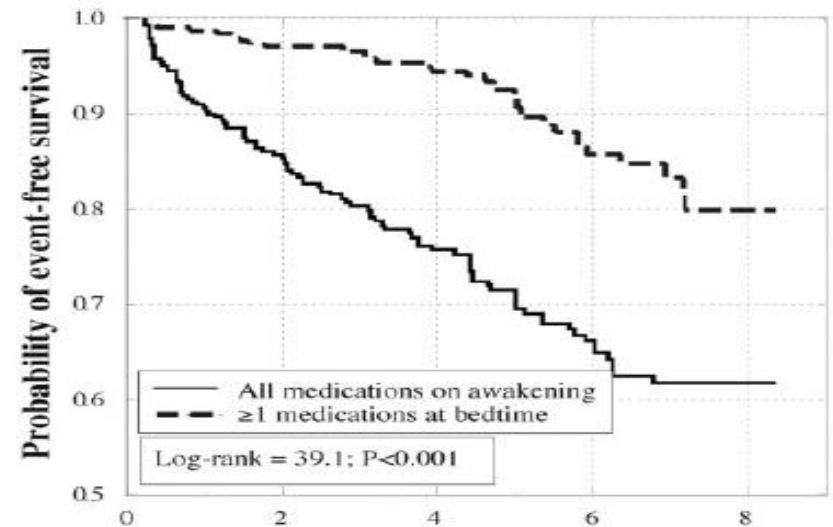
Time of ingestion of hypertension medications can affect circadian patterns of BP, but whether this translates into an effect on clinical outcomes is unknown. Here, in an open-label trial, we randomly assigned 661 patients with CKD either to take all prescribed hypertension medications upon awakening or to take at least one of them at bedtime. We measured 48-hour ambulatory BP at baseline and 3 months after any adjustment in treatment or, at the least, annually. After a median follow-up of 5.4 years, patients who took at least one BP-lowering medication at bedtime had an adjusted risk for total cardiovascular events (a composite of death, myocardial infarction, angina pectoris, revascularization, heart failure, arterial occlusion of lower extremities, occlusion of the retinal artery, and stroke) that was approximately one-third that of patients who took all medications upon awakening (adjusted HR 0.31; 95% CI 0.21 to 0.46; $P < 0.001$). Bedtime dosing demonstrated a similar significant reduction in risk for a composite outcome of cardiovascular death, myocardial infarction, and stroke (adjusted HR 0.28; 95% CI 0.13 to 0.61; $P < 0.001$). Furthermore, patients on bedtime treatment had a significantly lower mean sleep-time BP and a greater proportion demonstrated control of their ambulatory BP (56% versus 45%, $P = 0.003$). Each 5-mmHg decrease in mean sleep-time systolic BP was associated with a 14% reduction in the risk for cardiovascular events during follow-up ($P < 0.001$). In conclusion, among patients with CKD and hypertension, taking at least one antihypertensive medication at bedtime improves control of BP and reduces the risk for cardiovascular events.

J Am Soc Nephrol 22: 2313–2321, 2011. doi: 10.1681/ASN.2011040361

Bedtime Dosing of Antihypertensive Medications Reduces Cardiovascular Risk in CKD

Toplam KV Olaylar
















Major KV Olaylar
(KV ölümler, Mi, iskemik inme, hemorajik inme)



No. at risk	Duration of follow-up (years)				
	0	2	4	6	8
Awakening	332	264	180	118	
Bedtime	329	290	215	131	

Türk Hipertansiyon Uzlaşı Raporu 2019

2019 Turkish Hypertension Consensus Report

 Dr. Sinan Aydoğdu,¹  Dr. Kerim Güler,²  Dr. Fahri Bayram,³  Dr. Bülent Altun,⁴  Dr. Ülver Derici,⁵
 Dr. Adnan Abacı,⁶  Dr. Tufan Tükek,²  Dr. Tefvik Sabuncu,⁷  Dr. Mustafa Arıcı,⁴  Dr. Yunus Erdem,⁴
 Dr. Bülent Özin,⁸  Dr. İbrahim Şahin,⁹  Dr. Şehsuvar Ertürk,¹⁰  Dr. Atila Bitigen,¹¹  Dr. Lale Tokgözoğlu¹²

¹Türkiye Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, Ankara; ²İstanbul Üniversitesi İstanbul Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, İstanbul; ³Erciyes Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Endokrinoloji ve Metabolizma Bilim Dalı, Kayseri; ⁴Hacettepe Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Nefroloji Bilim Dalı, Ankara; ⁵Gazi Üniversitesi Tıp Fakültesi Hastanesi, İç Hastalıkları Anabilim Dalı, Nefroloji Bilim Dalı, Ankara; ⁶Gazi Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, Ankara; ⁷Harran Üniversitesi Tıp Fakültesi, Endokrinoloji ve Metabolizma Bilim Dalı, Şanlıurfa; ⁸Başkent Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, Ankara; ⁹İnönü Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Endokrinoloji ve Metabolizma Bilim Dalı, Malatya; ¹⁰Ankara Üniversitesi Tıp Fakültesi, İç Hastalıkları Anabilim Dalı, Nefroloji Bilim Dalı, Ankara; ¹¹Medical Park Fatih Hastanesi, Kardiyoloji Kliniği, İstanbul;

¹²Hacettepe Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, Ankara

Türk Hipertansiyon Uzlaşı Raporu 2019

Klinik Kan Basıncı Düzeylerine Göre Kan Basıncı Sınıflandırması

Kategori	SKB (mmHg)		DKB (mmHg)
Normal	<120	ve	<80
Artmış	120–139	ve/veya	80–89
Hipertansiyon	≥140	ve/veya	≥90
Evre 1	140–159	ve/veya	90–99
Evre 2	≥160	ve/veya	≥100

SKB: Sistolik kan basıncı; DKB: Diyastolik kan basıncı.

Türk Hipertansiyon Uzlaşı Raporu 2019

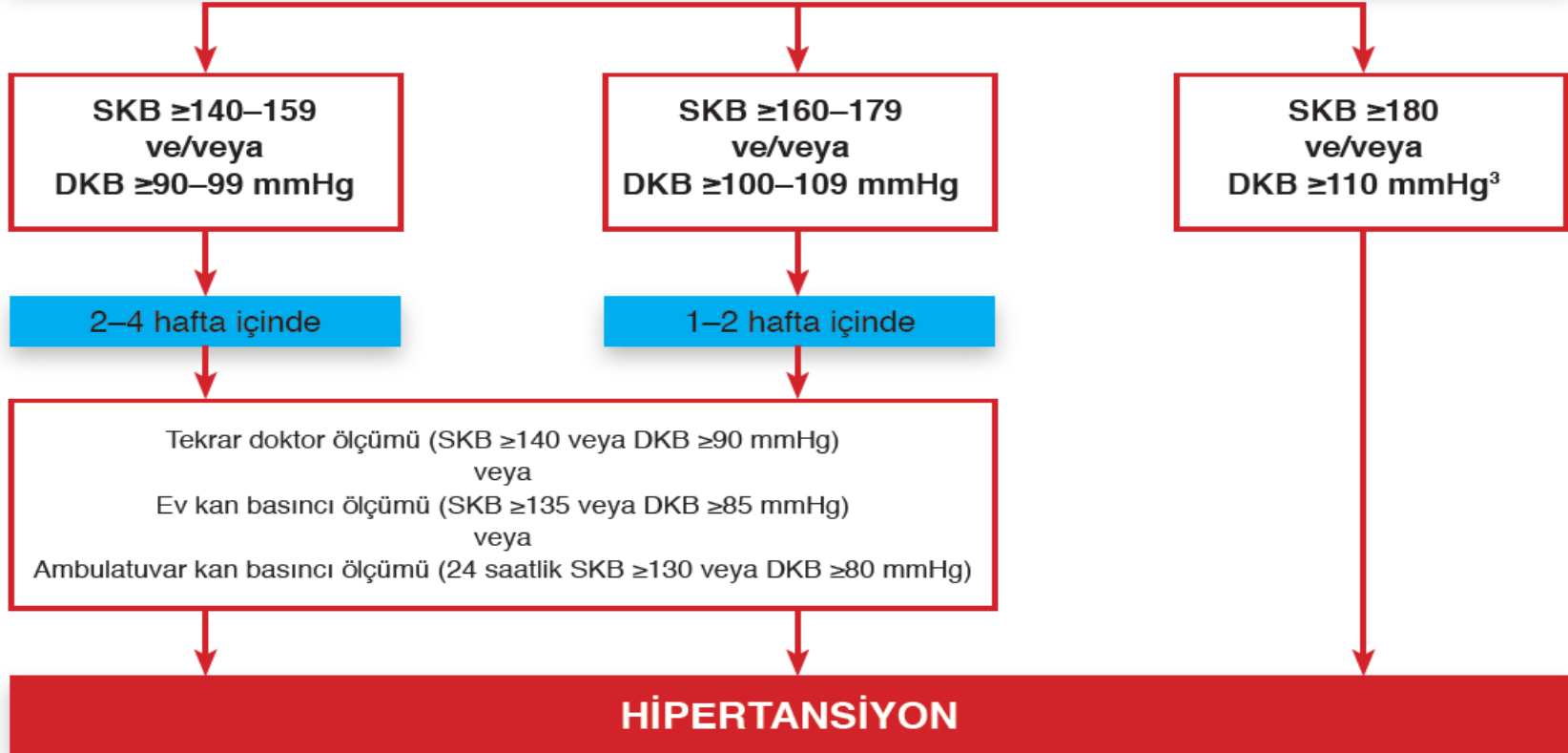
Ölçüm Yöntemine Göre Hipertansiyon Tanısı

Kategori	SKB (mmHg)		DKB (mmHg)
Klinik	≥140	ve/veya	≥90
Ev	≥135	ve/veya	≥85
Ambulatuvar kan basıncı			
24 saatlik ortalama	≥130	ve/veya	≥80
Gündüz ortalaması	≥135	ve/veya	≥85

SKB: Sistolik kan basıncı; DKB: Diyastolik kan basıncı.

Türk Hipertansiyon Uzlaşısı Raporu 2019

Klinik Kan Basıncı Ölçümü $\geq 140/90$ mmHg^{1,2}



¹Kan basıncı ölçümü ilk muayenede iki koldan ayrı ayrı yapılmalı ve takiplerde yüksek ölçülen kol kullanılmalıdır. En az iki ölçüm yaparak hastanın kan basıncı ortalamasına göre tanı akışı kullanılmalıdır.

²Bu ölçümler sırasında öykü, fizik muayene ve temel laboratuvar incelemelerinin yapılması önerilir. Ev kan basıncı veya ambulatuvar KB ölçümü imkanı olmayan hastalarda, laboratuvar sonuçlarını getirdikleri zaman yeniden ölçüm yapılarak tanı konulması önerilir.

³Hastanın kan basıncı bu değerlerde ise bir iki kez daha ölçülmelidir. Bu değerler devam ediyorsa, hastaya hipertansiyon tanısı hemen konulmalıdır.

SKB: Sistolik kan basıncı; DKB: Diyastolik kan basıncı.

Türk Hipertansiyon Uzlaşı Raporu 2019

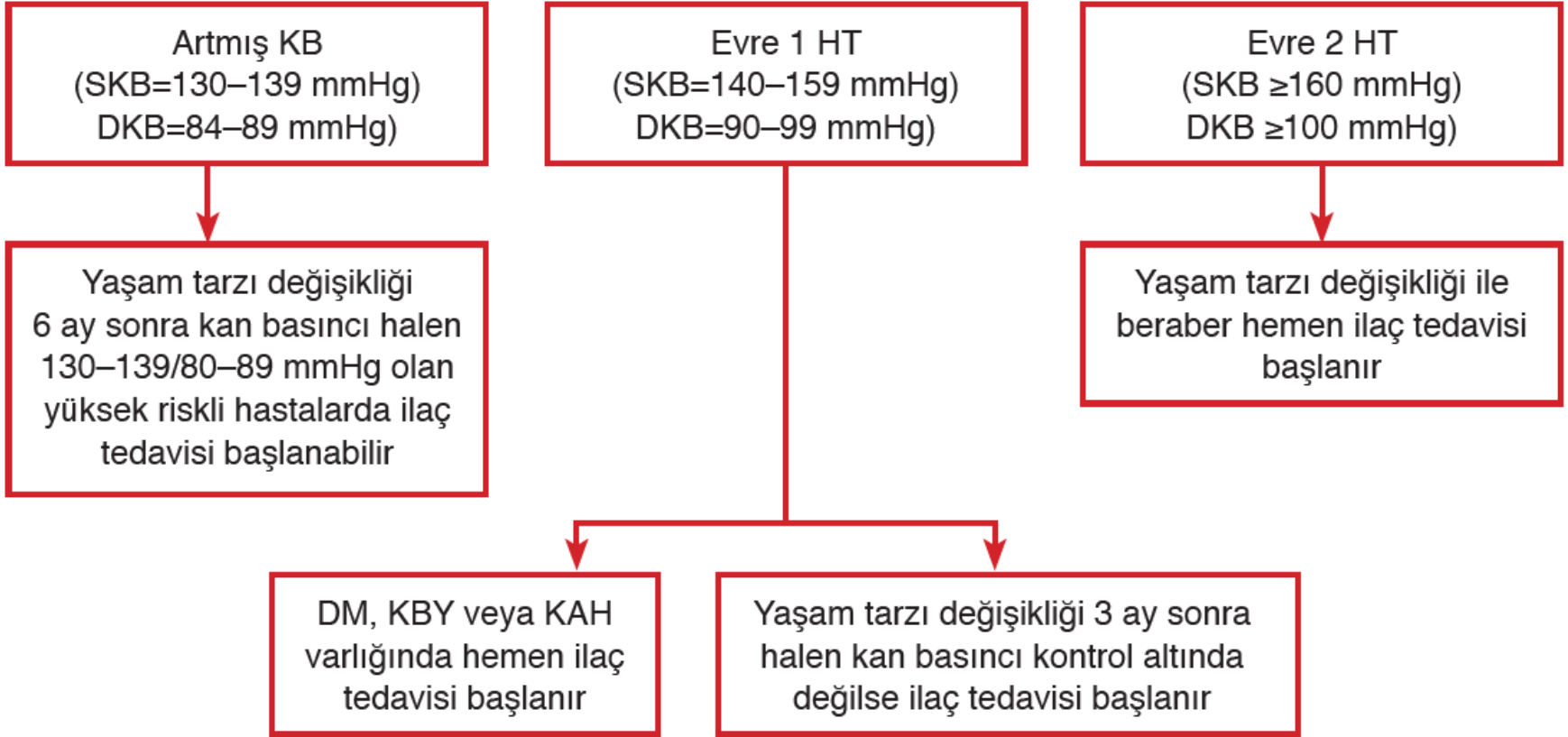
Yaşa Göre İlaç Tedavisi İçin Eşik ve Hedef Kan Basıncı Düzeyleri

Yaş grubu*	Eşik kan basıncı (mmHg)	Hedefkan basıncı (mmHg)
18–64 yaş	≥140/90	120–130/70–80
65–79 yaş	≥140/90	130–140/70–80
≥80 yaş	≥150	130–140/70–80

*Eşlik eden hastalık durumundan bağımsız olarak verilmiştir.

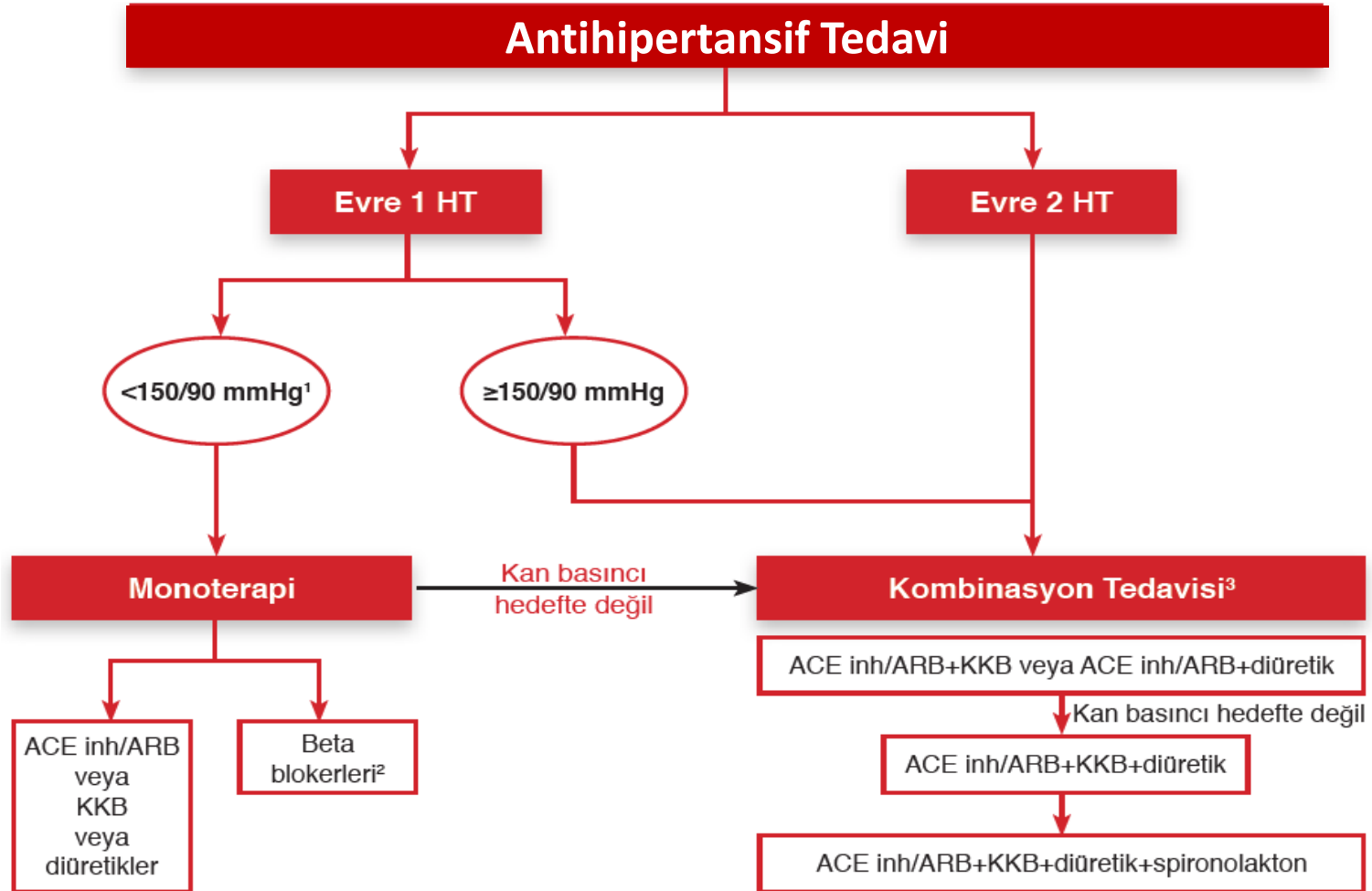
Türk Hipertansiyon Uzlaşısı Raporu 2019

Hipertansiyonda Tedavi Yaklaşımı



KB: Kan basıncı; SKB: Sistolik kan basıncı; DKB: Diyastolik kan basıncı; HT: Hipertansiyon; DM: Diyabetes mellitus; KBY: Kronik böbrek yetersizliği; KAH: Koroner arter hastalığı.

Türk Hipertansiyon Uzlaşısı Raporu 2019



¹Kan basıncı hedefinin ≤ 130 mmHg olduğu durumlarda doğrudan kombinasyon tedavisi başlanabilir.

²Betablokerler spesifik bir neden olması durumunda (KKY, KAH, angina pectoris veya gebelik planlayan hasta) başlanabilir.

³Üç veya dört ilaç gerektiren durumlarda tedavi etkinlik ve uyumunu artırmak için ilaçlardan en az birinin serbest doz kombinasyonu şeklinde ve sabit doz kombinasyondan farklı zamanda uygulanması (biri sabah diğeri akşam) önerilir.

HT: Hipertansiyon; ACE: Anjiyotensin dönüştürücü enzim; ARB: Anjiyotensin reseptör blokerleri; KKB: Kalsiyum kanal blokerleri.