ΥΠΕΡΤΑΣΗ

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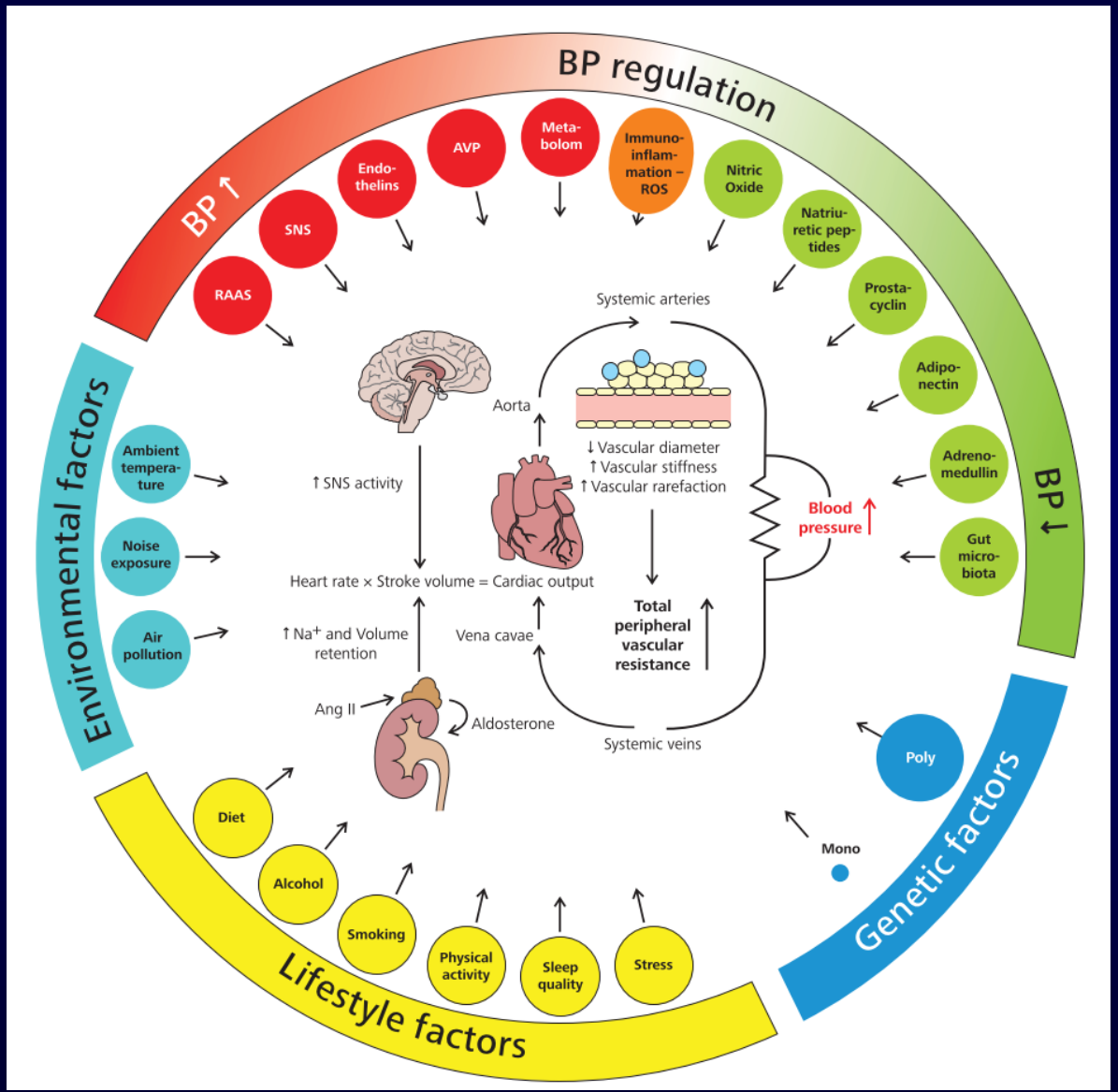
Αρτηριακή Υπέρταση

- **Primary (Essential) Hypertension**
- Secondary Hypertension (identifiable causes)
  - *Small fraction (<10%) of the overall hypertension prevalence*

Mechanisms involved in BP regulation and the pathophysiology of hypertension

Complex interaction between a genetic background, a large number of environmental factors and the aging process



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Ταξινόμηση ΑΠ & Βαθμού Υπέρτασης

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

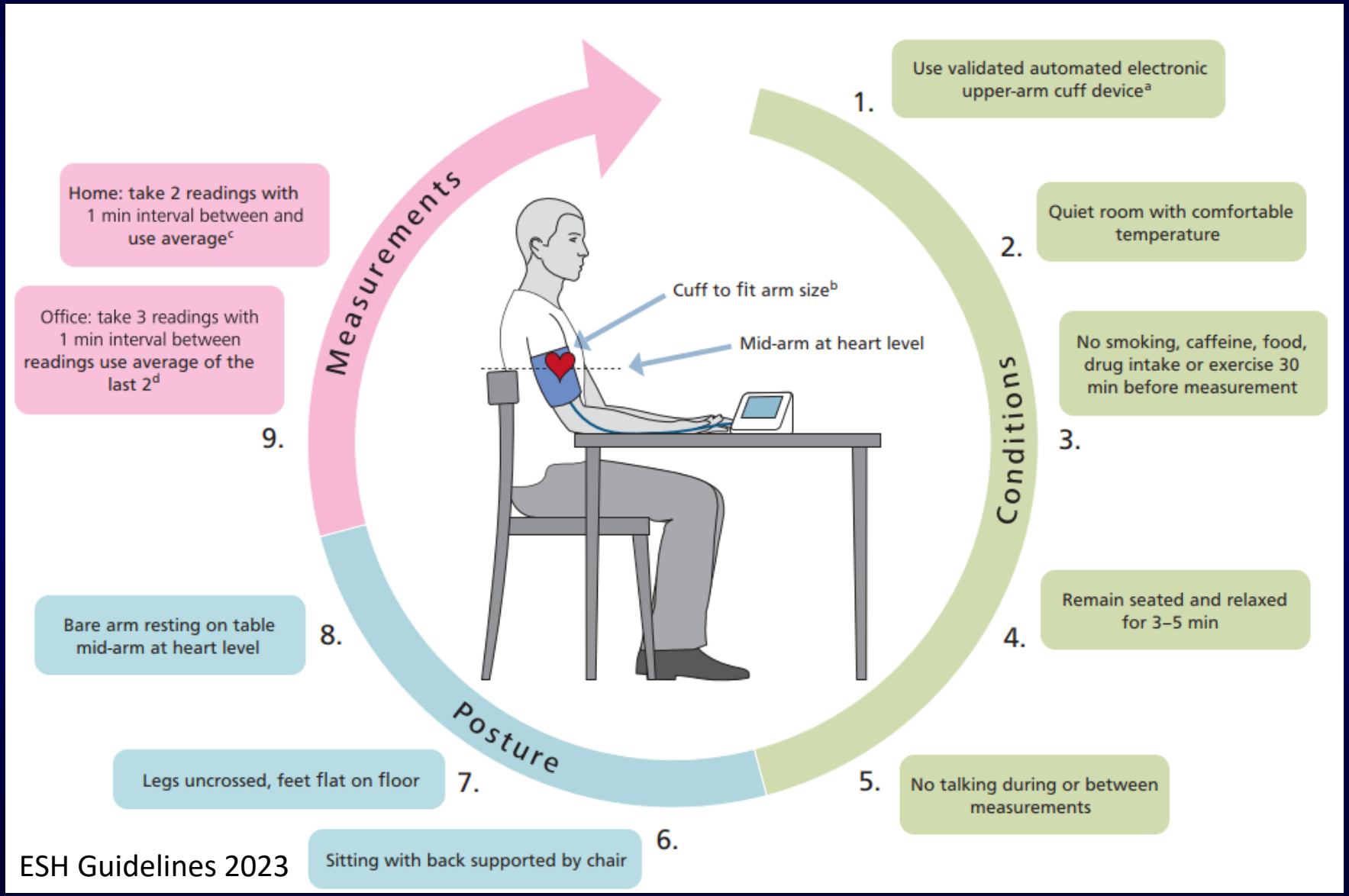
BP = blood pressure; SBP = systolic blood pressure.

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

[b]Isolated 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.

Recommendations for BP measurements in the office and at home



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Μετρήσεις

Μέθοδος	Στοιχεία
Ιατρείο	3 μετρήσεις,μέσος όρος 2ης και 3ης 5 min καθιστός, 2 βραχίονες
Holter	ΑΥ λευκής μπλούζας. Απουσία 10-20% πτώσης στον ύπνο→αυξημένος ΚΔ κίνδυνος
Ασθενής	Βοηθά μόνος του στη ρύθμιση της θεραπείας

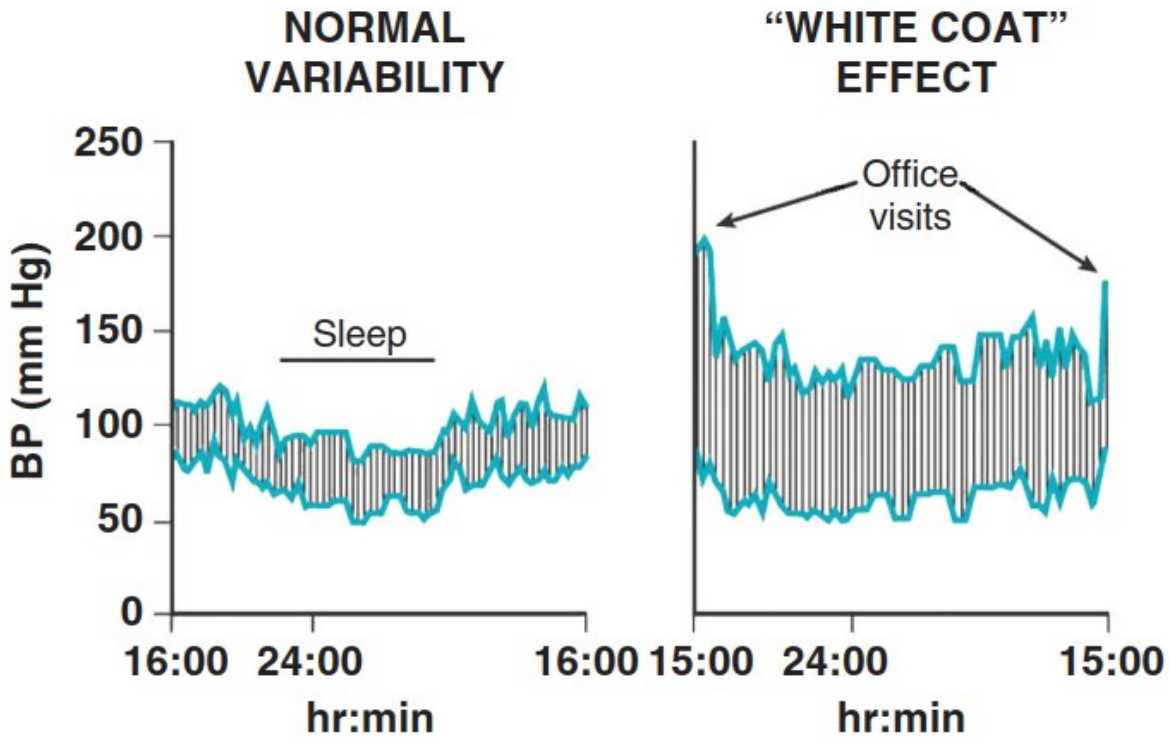


FIGURE e43-6 Twenty-four-hour ambulatory blood pressure (BP) monitor tracings in two different patients. **Left,** Optimal blood pressure in a healthy 37-year-old woman. Note the normal variability in blood pressure, the nocturnal dip in blood pressure during sleep, and the sharp increase in blood pressure on awakening. **Right,** Pronounced white coat effect in an 80-year-old woman referred for evaluation of medically refractory hypertension. Documentation of the white coat effect prevented overtreatment of the patient's isolated systolic hypertension. *(**Left**, Courtesy Dr. Ronald G. Victor, Heart Institute/Hypertension Center, Cedars-Sinai Medical Center, Los Angeles. **Right**, Provided by Dr. Wanpen Vongpatanasin, Hypertension Division, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas.)*

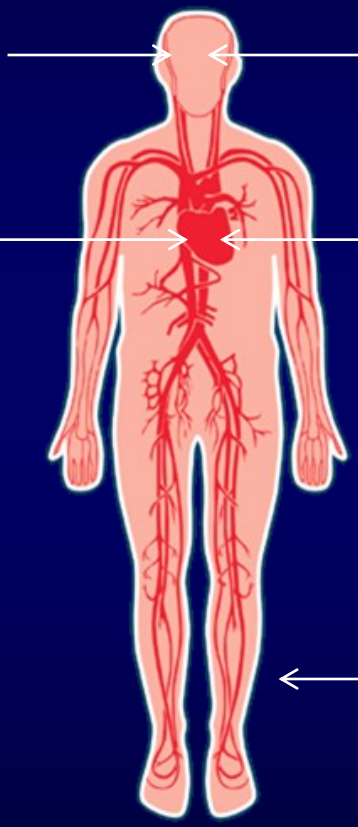
Γιατί πρέπει να θεραπεύεται η ΗΤΝ;

- **Βλάβη οργάνων στόχων** μέσω αθηροσκλήρυνσης
  - Σοβαρός και ανεξάρτητος παράγοντας καρδιαγγειακού κινδύνου
    - Γιατί προάγει την αθηροσκλήρυνση
      - Η αθηροσκλήρυνση/αθηροθρόμβωση προκαλεί οξέα στεφανιαία σύνδρομα, ΑΕΕ & περιφερική αγγειοπάθεια
- **Βλάβη οργάνων στόχων** με άλλους μηχανισμούς (LVH, νεφροπάθεια κτλ)

Μείζονες κλινικές εκδηλώσεις αθηροθρόμβωσης

Ισχαιμικό ΑΕΕ

Έμφραγμα

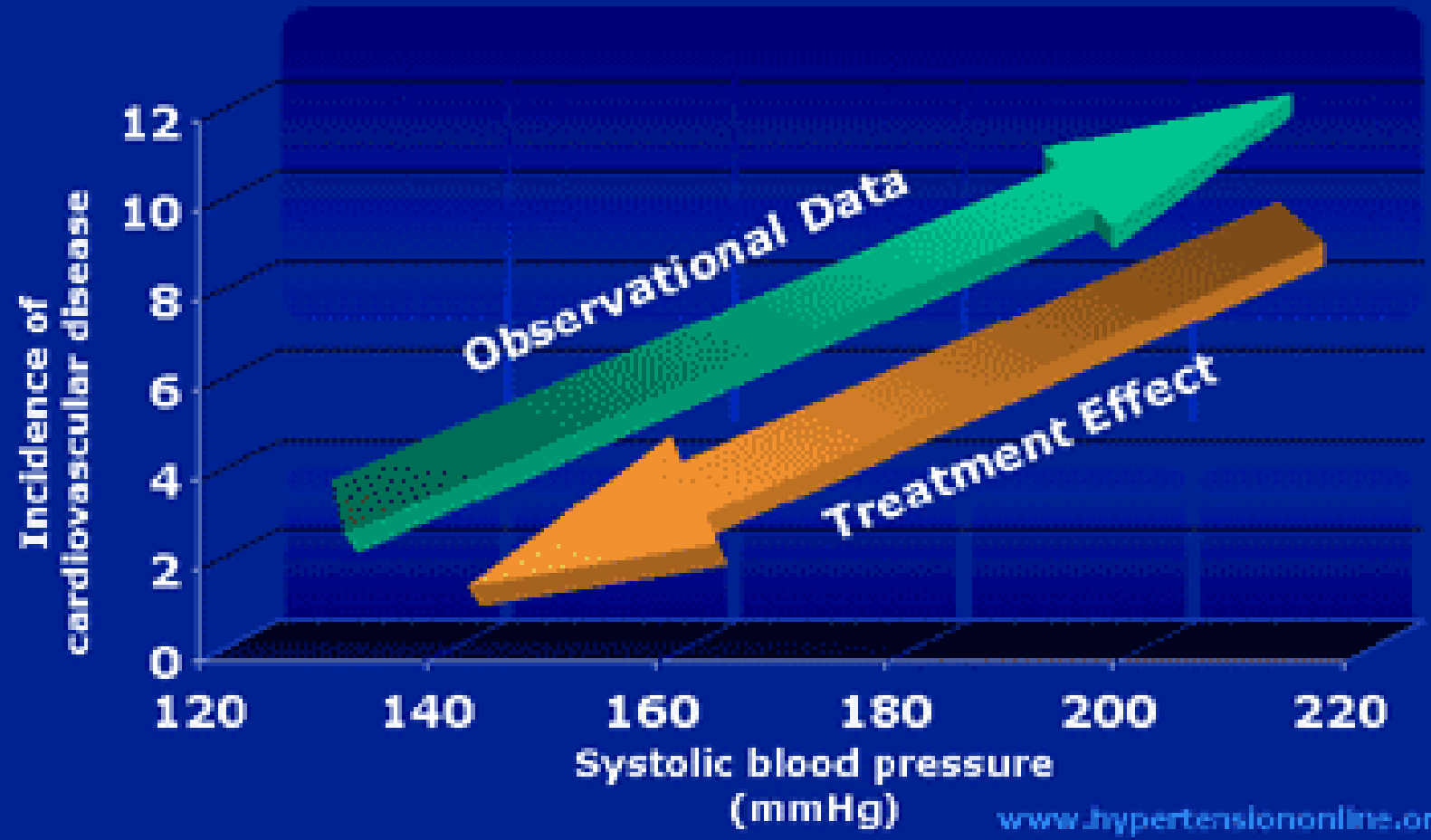


Παροδικό ισχαιμικό

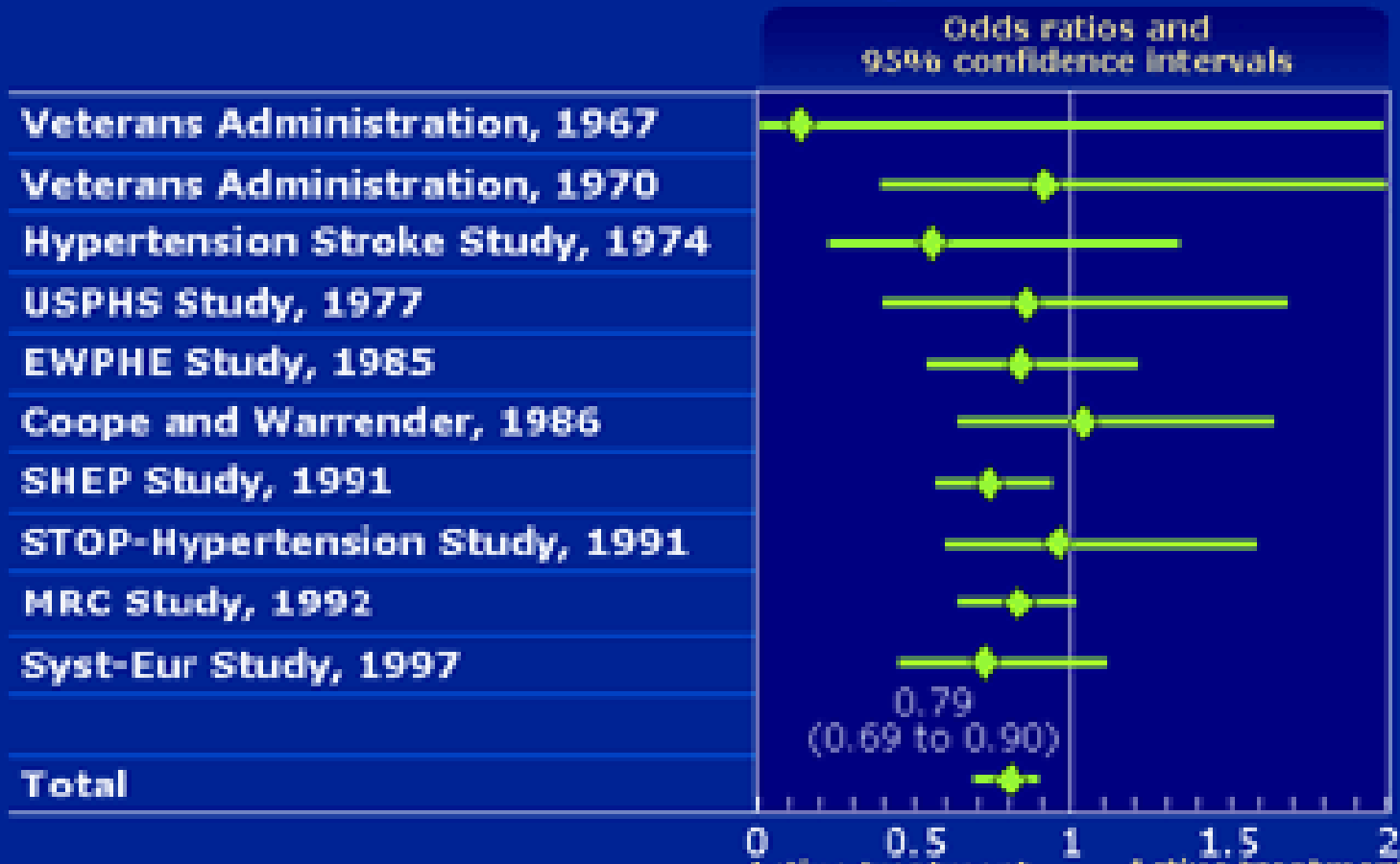
Στηθάγχη
- Σταθερή
- Ασταθής

Περιφερική αρτηριοπάθεια:
- Χωλότητα
- Πόνος ηρεμίας
- Γάγγραινα
- Νέκρωση

Hypertension Treatment Effect Mirrors Observational Data



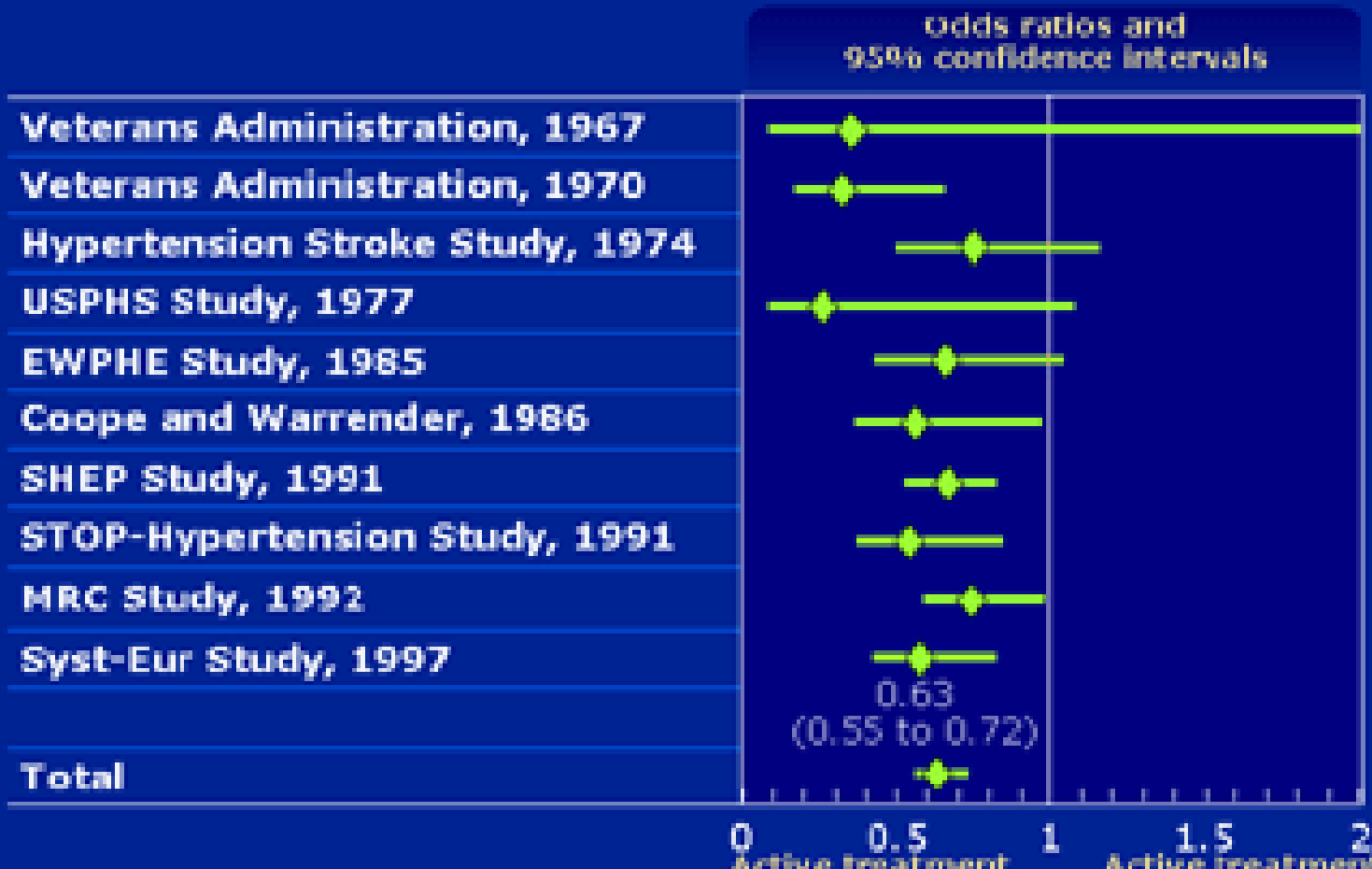
Relative Risk for Coronary Heart Disease



He J, et al. Am Heart J. 1999; 138:211-219.

www.hypertensiononline.org

Relative Risk for Stroke

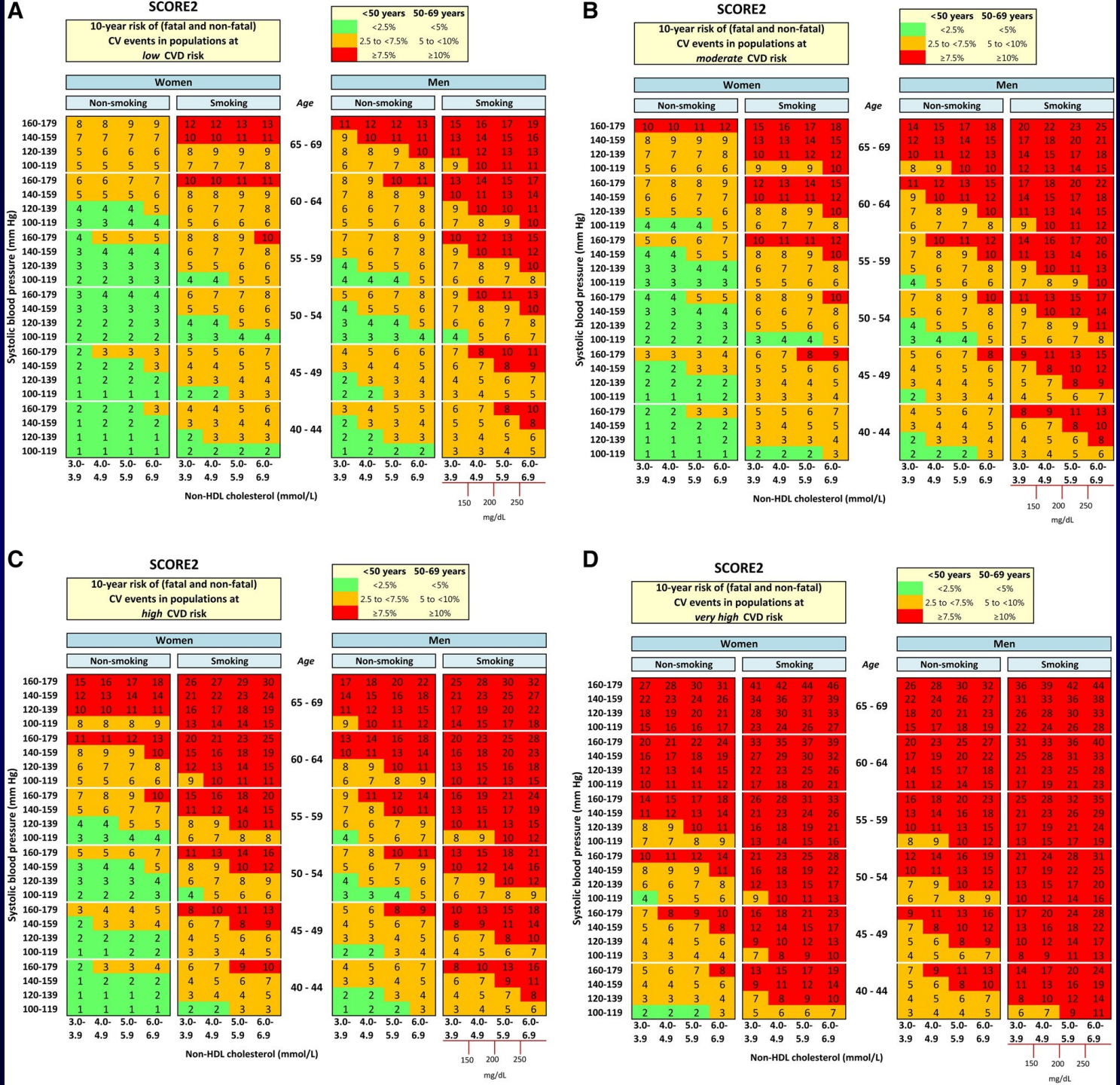


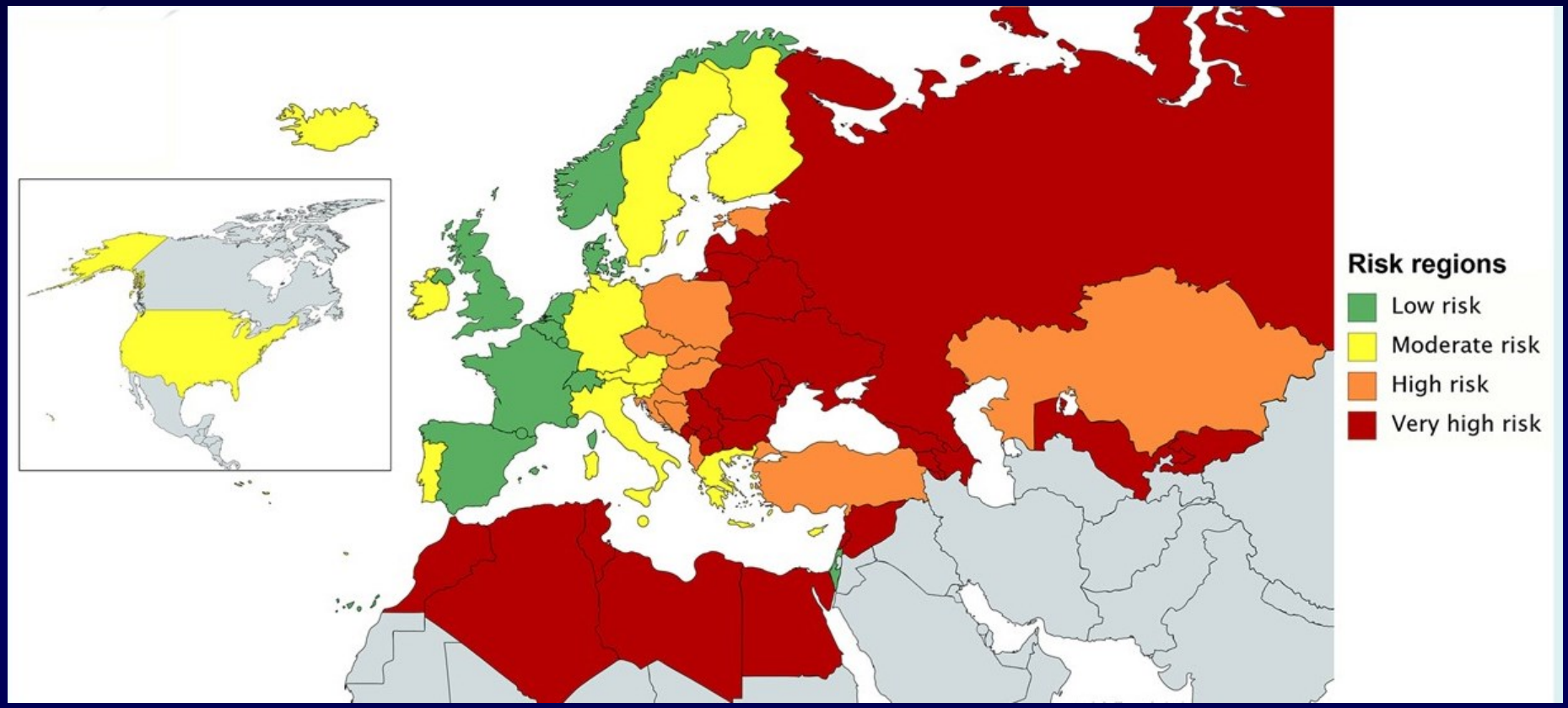
He J, et al. Am Heart J. 1999; 138:211-219.

Table 5 Ten year cardiovascular risk categories (Systematic COronary Risk Evaluation system)

Very high risk	**People with any of the following:**
	Documented CVD, either clinical or unequivocal on imaging. • **Clinical CVD** includes acute myocardial infarction, acute coronary syndrome, coronary or other arterial revascularization, stroke, TIA, aortic aneurysm, and PAD • **Unequivocal documented CVD on imaging** includes significant plaque (i.e. ≥50% stenosis) on angiography or ultrasound; it does not include increase in carotid intima-media thickness • **Diabetes mellitus with target organ damage**, e.g. proteinuria or a with a major risk factor such as grade 3 hypertension or hypercholesterolaemia • **Severe CKD** (eGFR <30 mL/min/1.73 m^2) • **A calculated 10 year SCORE of ≥10%**
High risk	**People with any of the following:** • **Marked elevation of a single risk factor**, particularly cholesterol >8 mmol/L (>310 mg/dL), e.g. familial hypercholesterolaemia or grade 3 hypertension (BP ≥180/110 mmHg) • **Most other people with diabetes mellitus** (except some young people with type 1 diabetes mellitus and without major risk factors, who may be at moderate-risk)
	Hypertensive LVH
	Moderate CKD eGFR 30-59 mL/min/1.73 m^2)
	A calculated 10 year SCORE of 5-10%
Moderate risk	**People with:** • **A calculated 10 year SCORE of ≥1 to <5%** • **Grade 2 hypertension** • **Many middle-aged people belong to this category**
Low risk	**People with:** • **A calculated 10 year SCORE of <1%**

BP = blood pressure; CKD = chronic kidney disease; CVD = cardiovascular disease; eGFR = estimated glomerular filtration rate; LVH = left ventricular hypertrophy; TIA = transient ischaemic attack; PAD = peripheral artery disease; SCORE = Systematic COronary Risk Evaluation.

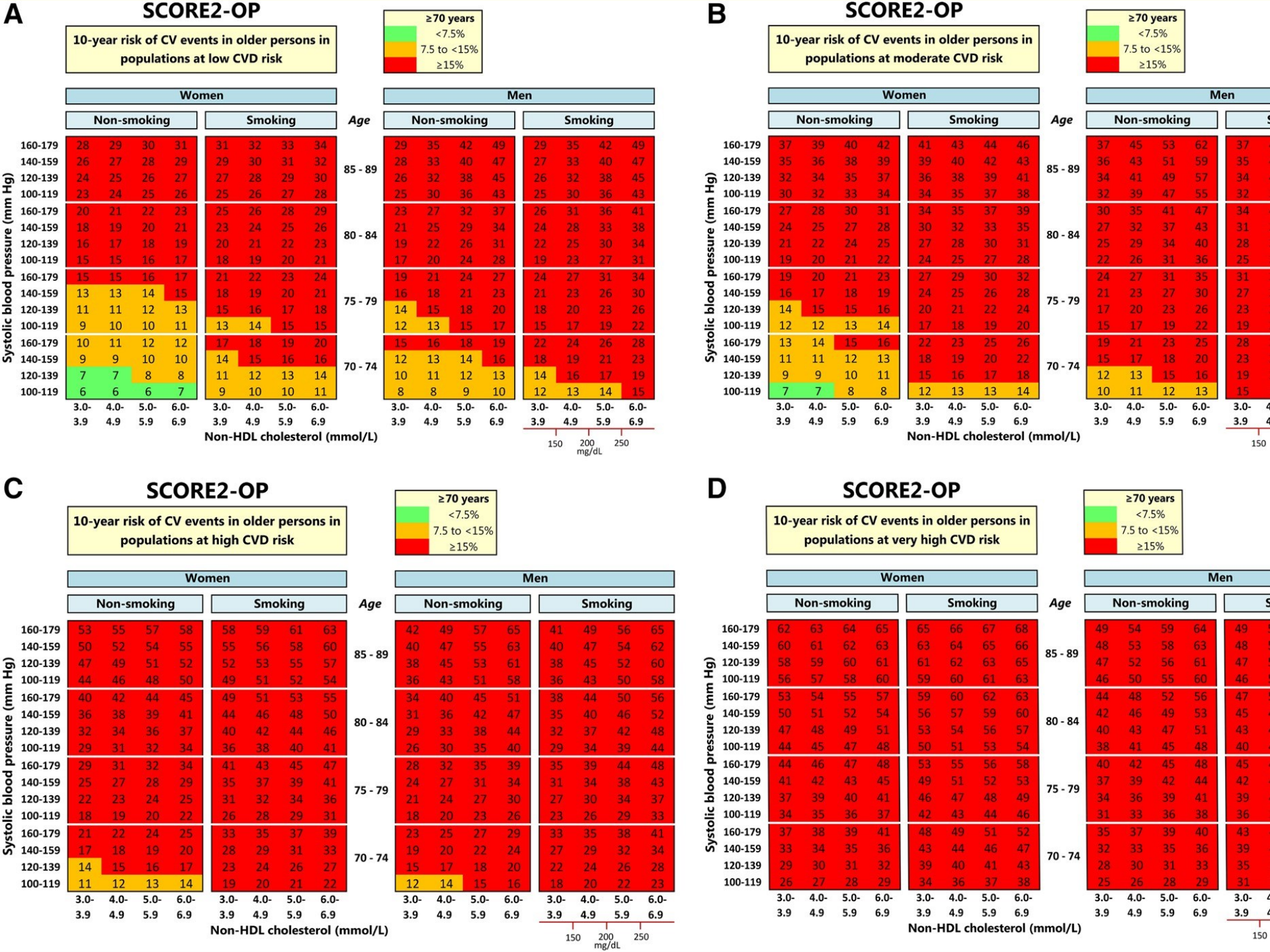

A
SCORE2
10-year risk of (fatal and non-fatal) CV events in populations at low CVD risk
<50 years 50-69 years
<2.5% <5%
2.5 to <7.5% 5 to <10%
≥7.5% ≥10%
Women
Men
Non-smoking
Smoking
Age
65 - 69
60 - 64
55 - 59
50 - 54
45 - 49
40 - 44
160-179 140-159 120-139 100-119
Systolic blood pressure (mm Hg)
3.0-3.9 4.0-4.9 5.0-5.9 6.0-6.9
Non-HDL cholesterol (mmol/L)
150 200 250
mg/dL
B
SCORE2
10-year risk of (fatal and non-fatal) CV events in populations at moderate CVD risk
C
SCORE2
10-year risk of (fatal and non-fatal) CV events in populations at high CVD risk
D
SCORE2
10-year risk of (fatal and non-fatal) CV events in populations at very high CVD risk



SCORE2 and SCORE2-OP interactive version

European Heart Journal, ehab312, https://doi.org/10.1093/eurheartj/ehab312

European Heart Journal, ehab309, https://doi.org/10.1093/eurheartj/ehab309


A
SCORE2-OP
10-year risk of CV events in older persons in populations at low CVD risk
≥70 years
<7.5%
7.5 to <15%
≥15%
Women
Men
Non-smoking
Smoking
Age
85 - 89
80 - 84
75 - 79
70 - 74
Systolic blood pressure (mm Hg)
160-179 28 29 30 31 | 31 32 33 34 | 29 35 42 49 | 29 35 42 49
140-159 26 27 28 29 | 29 30 31 32 | 28 33 40 47 | 27 33 40 47
120-139 24 25 26 27 | 27 28 29 30 | 26 32 38 45 | 26 32 38 45
100-119 23 24 25 26 | 25 26 27 28 | 25 30 36 43 | 25 30 36 43
160-179 20 21 22 23 | 25 26 28 29 | 23 27 32 37 | 26 31 36 41
140-159 18 19 20 21 | 23 24 25 26 | 21 25 29 34 | 24 28 33 38
120-139 16 17 18 19 | 20 21 22 23 | 19 22 26 31 | 22 25 30 34
100-119 15 15 16 17 | 18 19 20 21 | 17 20 24 28 | 19 23 27 31
160-179 15 15 16 17 | 21 22 23 24 | 19 21 24 27 | 24 27 31 34
140-159 13 13 14 15 | 18 19 20 21 | 16 18 21 23 | 21 23 26 30
120-139 11 11 12 13 | 15 16 17 18 | 14 15 18 20 | 18 20 23 26
100-119 9 10 10 11 | 13 14 15 15 | 12 13 15 17 | 15 17 19 22
160-179 10 11 12 12 | 17 18 19 20 | 15 16 18 19 | 22 24 26 28
140-159 9 9 10 10 | 14 15 16 16 | 12 13 14 16 | 18 19 21 23
120-139 7 7 8 8 | 11 12 13 14 | 10 11 12 13 | 14 16 17 19
100-119 6 6 6 7 | 9 10 10 11 | 8 8 9 10 | 12 13 14 15
3.0-3.9 4.0-4.9 5.0-5.9 6.0-6.9
Non-HDL cholesterol (mmol/L)
150 200 250
mg/dL
B
SCORE2-OP
10-year risk of CV events in older persons in populations at moderate CVD risk
≥70 years
<7.5%
7.5 to <15%
≥15%
Women
Men
Non-smoking
Smoking
Age
85 - 89
80 - 84
75 - 79
70 - 74
Systolic blood pressure (mm Hg)
160-179 37 39 40 42 | 41 43 44 46 | 37 45 53 62 | 37
140-159 35 36 38 39 | 39 40 42 43 | 36 43 51 59 | 35
120-139 32 34 35 37 | 36 38 39 41 | 34 41 49 57 | 34
100-119 30 32 33 34 | 34 35 37 38 | 32 39 47 55 | 32
160-179 27 28 30 31 | 34 35 37 39 | 30 35 41 47 | 34
140-159 24 25 27 28 | 30 32 33 35 | 27 32 37 43 | 31
120-139 21 22 24 25 | 27 28 30 31 | 25 29 34 40 | 28
100-119 19 20 21 22 | 24 25 27 28 | 22 26 31 36 | 25
160-179 19 20 21 23 | 27 29 30 32 | 24 27 31 35 | 31
140-159 16 17 18 19 | 24 25 26 28 | 21 23 27 30 | 27
120-139 14 15 15 16 | 20 21 22 24 | 17 20 23 26 | 23
100-119 12 12 13 14 | 17 18 19 20 | 15 17 19 22 | 19
160-179 13 14 15 16 | 22 23 25 26 | 19 21 23 25 | 28
140-159 11 11 12 13 | 18 19 20 22 | 15 17 18 20 | 23
120-139 9 9 10 11 | 15 16 17 18 | 12 13 15 16 | 19
100-119 7 7 8 8 | 12 13 13 14 | 10 11 12 13 | 15
3.0-3.9 4.0-4.9 5.0-5.9 6.0-6.9
Non-HDL cholesterol (mmol/L)
150
C
SCORE2-OP
10-year risk of CV events in older persons in populations at high CVD risk
≥70 years
<7.5%
7.5 to <15%
≥15%
Women
Men
Non-smoking
Smoking
Age
85 - 89
80 - 84
75 - 79
70 - 74
Systolic blood pressure (mm Hg)
160-179 53 55 57 58 | 58 59 61 63 | 42 49 57 65 | 41 49 56 65
140-159 50 52 54 55 | 55 56 58 60 | 40 47 55 63 | 40 47 54 62
120-139 47 49 51 52 | 52 53 55 57 | 38 45 53 61 | 38 45 52 60
100-119 44 46 48 50 | 49 51 52 54 | 36 43 51 58 | 36 43 50 58
160-179 40 42 44 45 | 49 51 53 55 | 34 40 45 51 | 38 44 50 56
140-159 36 38 39 41 | 44 46 48 50 | 31 36 42 47 | 35 40 46 52
120-139 32 34 36 37 | 40 42 44 46 | 29 33 38 44 | 32 37 42 48
100-119 29 31 32 34 | 36 38 40 41 | 26 30 35 40 | 29 34 39 44
160-179 29 31 32 34 | 41 43 45 47 | 28 32 35 39 | 35 39 44 48
140-159 25 27 28 29 | 35 37 39 41 | 24 27 31 34 | 31 34 38 43
120-139 22 23 24 25 | 31 32 34 36 | 21 24 27 30 | 27 30 34 37
100-119 18 19 20 22 | 26 28 29 31 | 18 20 23 26 | 23 26 29 33
160-179 21 22 24 25 | 33 35 37 39 | 23 25 27 29 | 33 35 38 41
140-159 17 18 19 20 | 28 29 31 33 | 19 20 22 24 | 27 29 32 34
120-139 14 15 16 17 | 23 24 26 27 | 15 17 18 20 | 22 24 26 28
100-119 11 12 13 14 | 19 20 21 22 | 12 14 15 16 | 18 20 22 23
3.0-3.9 4.0-4.9 5.0-5.9 6.0-6.9
Non-HDL cholesterol (mmol/L)
150 200 250
mg/dL
D
SCORE2-OP
10-year risk of CV events in older persons in populations at very high CVD risk
≥70 years
<7.5%
7.5 to <15%
≥15%
Women
Men
Non-smoking
Smoking
Age
85 - 89
80 - 84
75 - 79
70 - 74
Systolic blood pressure (mm Hg)
160-179 62 63 64 65 | 65 66 67 68 | 49 54 59 64 | 49
140-159 60 61 62 63 | 63 64 65 66 | 48 53 58 63 | 48
120-139 58 59 60 61 | 61 62 63 65 | 47 52 56 61 | 47
100-119 56 57 58 60 | 59 60 61 63 | 46 50 55 60 | 46
160-179 53 54 55 57 | 59 60 62 63 | 44 48 52 56 | 47
140-159 50 51 52 54 | 56 57 59 60 | 42 46 49 53 | 45
120-139 47 48 49 51 | 53 54 56 57 | 40 43 47 51 | 43
100-119 44 45 47 48 | 50 51 53 54 | 38 41 45 48 | 40
160-179 44 46 47 48 | 53 55 56 58 | 40 42 45 48 | 45
140-159 41 42 43 45 | 49 51 52 53 | 37 39 42 44 | 42
120-139 37 39 40 41 | 46 47 48 49 | 34 36 39 41 | 39
100-119 34 35 36 37 | 42 43 44 46 | 31 33 36 38 | 36
160-179 37 38 39 41 | 48 49 51 52 | 35 37 39 40 | 43
140-159 33 34 35 36 | 43 44 46 47 | 32 33 35 36 | 39
120-139 29 30 31 32 | 39 40 41 43 | 28 30 31 33 | 35
100-119 26 27 28 29 | 34 36 37 38 | 25 26 28 29 | 31
3.0-3.9 4.0-4.9 5.0-5.9 6.0-6.9
Non-HDL cholesterol (mmol/L)
150

Cardiovascular risk according to grade and stage of hypertension

Hypertension disease staging	Other risk factors, HMOD, CVD or CKD	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 ≥ 180 DBP ≥ 110
Stage 1	No other risk factors[a]	Low risk	Low risk	Moderate risk	High risk
	1 or 2 risk factors	Low risk	Moderate risk	Moderate to high risk	High risk
	≥3 risk factors	Low to moderate risk	Moderate to high risk	High risk	High risk
Stage 2	HMOD, CKD grade 3, or diabetes mellitus	Moderate to high risk	High risk	High risk	Very high risk
Stage 3	Established CVD or CKD grade ≥4	Very high risk	Very high risk	Very high risk	Very high risk

	<50 years	60–69 years	≥70 years
	<2.5%	<5%	<7.5%
	2.5 to <7.5%	5 to <10%	7.5 to <15%
	≥7.5%	≥10%	≥15%

Complementary risk estimation in Stage 1 with SCORE2/SCOR2-OP

Recommendations and statements	CoR	LoE
CV risk assessment with the SCORE2 and SCOR2-OP system is recommended for hypertensive patients who are not already at high or very high risk due to established CVD or CKD, long-lasting or complicated diabetes, severe HMOD (e.g. LVH) or a markedly elevated single risk factor (e.g. cholesterol, albuminuria).	I	B

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Παράγοντες που επηρεάζουν τον καρδιαγγειακό κίνδυνο και την πρόγνωση των ασθενών με ΑΥ

Demographic characteristics and laboratory parameters
Sex[a] (men >women)
Age[a]
Smoking (current or past history)[a]
Total cholesterol[a] and HDL-C
Uric acid
Diabetes[a]
Overweight or obesity
Family history of premature CVD (men aged <55 years and women aged <65 years)
Family or parental history of early-onset hypertension
Early-onset menopause
Sedentary lifestyle
Psychosocial and socioeconomic factors
Heart rate (resting values >80 beats/min)
Asymptomatic HMOD
Arterial stiffening: Pulse pressure (in older people) ≥60 mmHg Carotid–femoral PWV >10 m/s
ECG LVH (Sokolow–Lyon index >35 mm, or R in aVL ≥11 mm; Cornell voltage duration product >2440 mm.ms, or Cornell voltage >28 mm in men or >20 mm in women)
Echocardiographic LVH [LV mass index: men >50 g/m$^{2.7}$; women >47 g/m$^{2.7}$ (height in m$^{2.7}$); indexation for BSA may be used in normal-weight patients; LV mass/BSA g/m^2 >115 (men) and >95 (women)]
Microalbuminuria (30–300 mg/24 h), or elevated albumin–creatinine ratio (30–300 mg/g; 3.4–34 mg/mmol) (preferentially on morning spot urine)[b]
Moderate CKD with eGFR >30–59 mL/min/1.73 m^2 (BSA) or severe CKD eGFR <30 mL/min/1.73 m^2 [b]
Ankle-brachial index <0.9
Advanced retinopathy: haemorrhages or exudates, papilloedema
Established CV or renal disease
Cerebrovascular disease: ischaemic stroke, cerebral haemorrhage, TIA
CAD: myocardial infarction, angina, myocardial revascularization
Presence of atheromatous plaque on imaging
Heart failure, including HFpEF
Peripheral artery disease
Atrial fibrillation

BSA = body surface area; CAD = coronary artery disease; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovascular disease; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; HDL-C = HDL cholesterol; HFpEF = heart failure with preserved ejection fraction; HMOD = hypertension-mediated organ damage; LV = left ventricular; LVH = left ventricular hypertrophy; PWV = pulse wave velocity; SCORE = Systematic COronary Risk Evaluation; TIA = transient ischaemic attack.
[a]CV risk factors included in the SCORE system.
[b]Proteinuria and reduced eGFR are independent risk factors.

Όφελος από μείωση ΑΠ

	% Μείωση
ΑΕΕ	35–40%
Έμφραγμα	20–25%
Καρδιακή ανεπάρκεια	50%

Όφελος από μείωση ΑΠ

Σε σταδίου 1 HTN &
συνοδούς CVD risk factors,
μείωση κατά 12 mmHg της SBP για
10 years => αποφυγή 1 θανάτου ανά 11
ασθενείς

BP Control Rates

Trends in awareness, treatment, and control of high blood pressure in adults ages 18–74

	National Health and Nutrition Examination Survey, Percent			
	II 1976–80	II (Phase 1) 1988–91	II (Phase 2) 1991–94	1999–2000
Awareness	51	73	68	70
Treatment	31	55	54	59
Control	10	29	27	34

Sources: Unpublished data for 1999–2000 computed by M. Wolz, National Heart, Lung, and Blood Institute; JNC 6.

ΔΙΕΡΕΥΝΗΣΗ ΑΣΘΕΝΟΥΣ ΜΕ ΠΙΘΑΝΗ Η' ΕΓΚΑΤΕΣΤΗΜΕΝΗ ΑΥ

Αρχική Εκτίμηση – Διερεύνηση Ασθενούς

Τρείς στόχοι:

1. Έλεγχος συνηθειών & έξεων, αναγνώριση άλλων παραγόντων κινδύνου και συνοδών νόσων

2. Διάγνωση δευτερογενούς ΗΤΝ

3. Διάγνωση ύπαρξης βλάβης στα όργανα στόχους και ύπαρξης καρδιαγγειακής νόσου

ΑΥ: ΙΣΤΟΡΙΚΟ

Personal history
- Time of the first diagnosis of hypertension, including records of any previous medical screening, hospitalization
- Stable or rapidly increasing BP
- Recordings of current and past BP values by self BP measurements
- Current/past antihypertensive medications including their effectiveness and intolerance
- Adherence to therapy
- Previous hypertension in pregnancy/preeclampsia

Risk factors[a]
- Family history of hypertension, CVD, stroke or kidney disease
- Smoking history
- Dietary history, alcohol consumption
- Lack of physical exercise/sedentary lifestyle
- Weight gain or loss in the past
- History of erectile dysfunction
- Sleep history, snoring, sleep apnea (information also from partner)
- Distress or eustress with job or at home (subjective stress level)
- Long-term cancer survivor

History and symptoms of HMOD, CVD, stroke and kidney disease
- Brain and eyes: headache, vertigo, syncope, impaired vision, TIA, sensory or motor deficit, stroke, carotid revascularization, cognitive impairment, memory loss, dementia (in older people)
- Heart: chest pain, shortness of breath, edema, myocardial infarction, coronary revascularization, syncope, history of palpitations, arrhythmias (especially AF), heart failure
- Kidney: thirst, polyuria, nocturia, hematuria, urinary tract infections
- Peripheral arteries: cold extremities, intermittent claudication, pain-free walking distance, pain at rest, ulcer or necrosis, peripheral revascularization
- Patient or family history of CKD (e.g. polycystic kidney disease)

History of possible secondary hypertension
- Young onset of grade 2 or 3 hypertension (<40 years), or sudden development of hypertension or rapidly worsening BP in older patients
- History of repetitive renal/urinary tract disease
- Repetitive episodes of sweating, headache, anxiety or palpitations, suggestive of pheochromocytoma
- History of spontaneous or diuretic-provoked hypokalemia, episodes of muscle weakness and tetany (hyperaldosteronism)
- Symptoms suggestive of thyroid disease or hyperparathyroidism
- History of or current pregnancy, postmenopausal status and oral contraceptive use or hormonal substitution

Drug treatments or use (other than antihypertensive drugs)
- Recreational drug/substance abuse, concurrent therapies including nonprescription drugs, e.g. glucocorticoids, NSAIDs/COX-2 inhibitors, paracetamol (acetaminophen), immunosuppressive drugs, anticancer drugs, nasal vasoconstrictors

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ΑΥ: ΦΥΣΙΚΗ ΕΞΕΤΑΣΗ

Body habitus
• Weight and height measured on a calibrated scale, with calculation of BMI
• Waist circumference
Signs of hypertension-mediated organ damage
• Neurological examination and cognitive status
• Fundoscopic examination for hypertensive retinopathy in emergencies
• Auscultation of heart and carotid arteries
• Palpation of carotid and peripheral arteries
• Ankle–brachial index
Signs of secondary hypertension (Section 6)
• Skin inspection: cafe-au-lait patches of neurofibromatosis (pheochromocytoma)
• Kidney palpation for signs of renal enlargement in polycystic kidney disease
• Auscultation of heart and renal arteries for murmurs or bruits indicative of aortic coarctation, or renovascular hypertension
• Signs of Cushing's disease or acromegaly
• Signs of thyroid disease

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Παράγοντες ΚΔ κινδύνου

- Υπέρταση*
- Κάπνισμα
- Παχυσαρκία* (BMI $\geq$30 kg/m^2)
- Καθιστική ζωή
- Δυσλιπιδαιμία*
- Διαβήτης*
- Μικραλβουμινουρία ή GFR <60 ml/min
- Ηλικία (> 55 Α, 65 Γ)
- Οικογενειακό ιστορικό CVD
  (Α< 55 ή Γ<65)

*Μεταβολικό σύνδρομο

Δευτεροπαθής ΑΥ

- Sleep apnea
- Παρεγχυματική νόσος νεφρών (ΧΝΑ, πολυκυστική νόσος)
- Νεφραγγειακή νόσος (αθηροσκλήρωση, ινομυώδης δυπλασία)
- Πρωτοπαθής αλδοστερονισμός
- Φαιοχρωμοκύτωμα
- Στεροειδή και Cushing's syndrome
- Στένωση ισθμού αορτής
- Θυρεο/παραθυρεο-ειδής
- Φάρμακα (αντισυλληπτικά, ΜΣΑΦ, SNRI: Serotonin and norepinephrine reuptake inhibitors, στεροειδή)

Κοινά Αίτια Δευτεροπαθούς ΑΥ

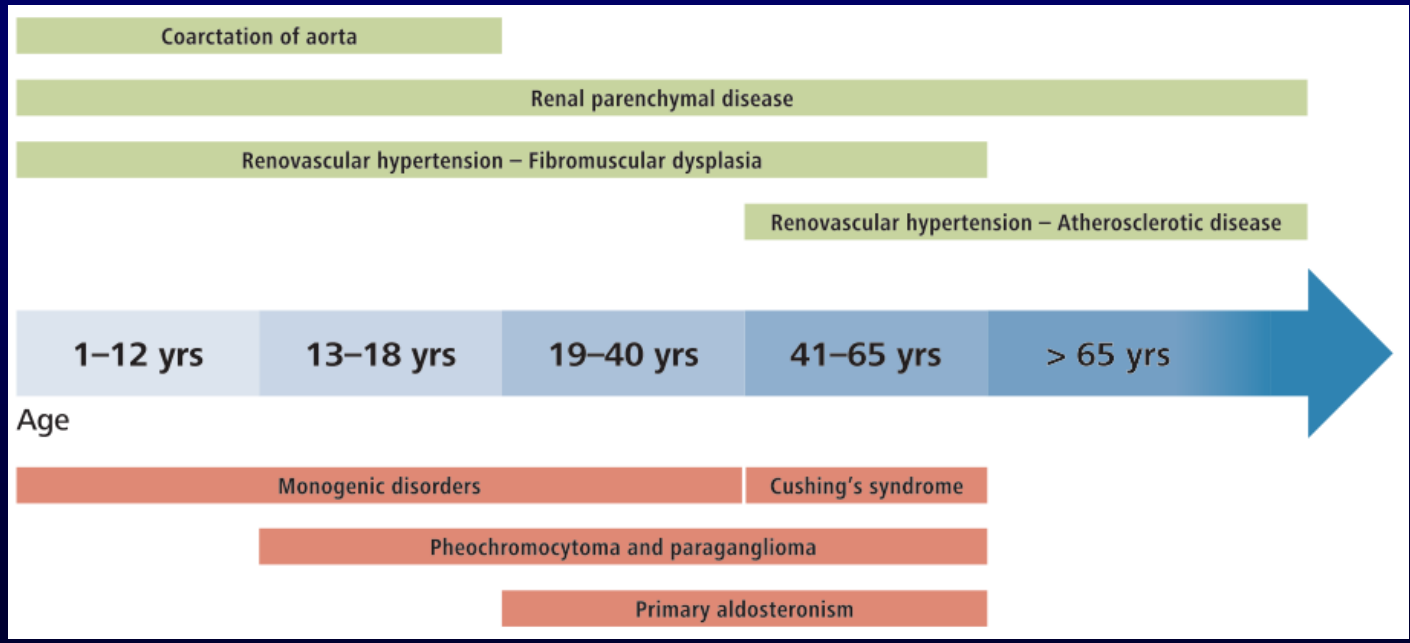
Cause	Prevalence in hypertensive patients	Suggestive symptoms and signs	Screening Investigations
Obstructive sleep apnoea	5–10%	Snoring; obesity (can be present in non-obese); morning headache; daytime somnolence	Epworth score and ambulatory polygraphy
Renal parenchymal disease	2–10%	Mostly asymptomatic; diabetes; haematuria, proteinuria, nocturia; anaemia, renal mass in adult polycystic CKD	Plasma creatinine and electrolytes, eGFR; urine dipstick for blood and protein, urinary albumin:creatinine ratio; renal ultrasound
Renovascular disease			
Atherosclerotic renovascular disease	1–10%	Older; widespread atherosclerosis (especially PAD); diabetes; smoking; recurrent flash pulmonary oedema; abdominal bruit	Duplex renal artery Doppler or CT angiography or MR angiography
Fibromuscular dysplasia		Younger; more common in women; abdominal bruit	
Endocrine causes			
Primary Aldosteronism	5 - 15%	Mostly asymptomatic; muscle weakness (rare)	Plasma aldosterone and renin, and aldosterone:renin ratio; hypokalaemia (in a minority): note hypokalaemia can depress aldosterone levels
Phaeochromocytoma	<1%	Episodic symptoms (the 5 'Ps'): paroxysmal hypertension, pounding headache, perspiration, palpitations, and pallor; labile BP; BP surges precipitated by drugs (e.g. beta-blockers, metoclopramide, sympathomimetics, opioids, and tricyclic antidepressants)	Plasma or 24 h urinary fractionated metanephrines
Cushing's syndrome	<1%	Moon face, central obesity, skin atrophy, striae and bruising; diabetes; chronic steroid use	24 h urinary-free cortisol
Thyroid disease (hyper- or hypothyroidism)	1 - 2%	Signs and symptom of hyper- or hypothyroidism	Thyroid function tests
Hyperparathyroidism	<1%	Hypercalcaemia, hypophosphataemia	Parathyroid hormone, Ca^{2+}
Other causes			
Coarctation of the aorta	<1%	Usually detected in children or adolescence; different BP (≥20/10 mmHg) between upper–lower extremities and/or between right–left arm and delayed radial-femoral femoral pulsation; low ABI interscapular ejection murmur; rib notching on chest X-ray	Echocardiogram

ABI = ankle-brachial index; BP = blood pressure; CKD = chronic kidney disease; CT = computed tomography; eGFR = estimated glomerular filtration rate; MR = magnetic resonance; PAD = peripheral artery disease.

Χαρακτηριστικά Ασθενών και Πιθανή 2παθής ΑΥ

Younger patients (<40 years) with grade 2 or 3 hypertension or hypertension of any grade in childhood
Sudden onset of hypertension in individuals with previously documented normotension
Acute worsening of BP control in patients with previously well controlled by treatment
True resistant hypertension hypertension
Hypertensive emergency
Severe (grade 3) or malignant hypertension
Severe and/or extensive HMOD, particularly if disproportionate for the duration and severity of the BP elevation
Clinical or biochemical features suggestive of endocrine causes of hypertension
Clinical features suggestive of atherosclerotic renovascular disease or fibromuscular dysplasia
Clinical features suggestive of obstructive sleep apnea
Severe hypertension in pregnancy (>160/110 mmHg) or acute worsening of BP control in pregnant women with preexisting hypertension

Αίτια 2παθούς ΑΥ και Ηλικία ασθενούς



Έλεγχος για Αίτια 2παθούς ΑΥ

DIAGNOSIS	DIAGNOSTIC PROCEDURE(S)	
	Initial	Additional
Chronic renal disease	Urinalysis, serum creatinine, renal sonography	Isotopic renography, renal biopsy
Renovascular disease	Renal sonography (atrophic kidney)	Magnetic resonance or computed tomography (CT) angiography, Duplex Doppler sonography, digital subtraction renal angiography
Coarctation	Blood pressure in legs	Echocardiography, magnetic resonance imaging, aortography
Primary aldosteronism	Plasma renin, serum aldosterone	Salt loading, adrenal vein sampling
Cushing syndrome	1-mg dexamethasone suppression test	Urinary cortisol after variable doses of dexamethasone, adrenal CT, scintiscans
Pheochromocytoma	Plasma-free metanephrines	24-hour urinary metanephrines and catecholamines, adrenal CT

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Αθηροσκληρυντική Νεφραγγειακή Νόσος

Prevalence:
6–14%[a]

Suggestive symptoms, signs and findings

Resistant hypertension
Flash pulmonary edema
Rapidly declining kidney function
Acute renal function degradation on ACEi or ARB
Generalized atherosclerosis[b]

1st choice screening test

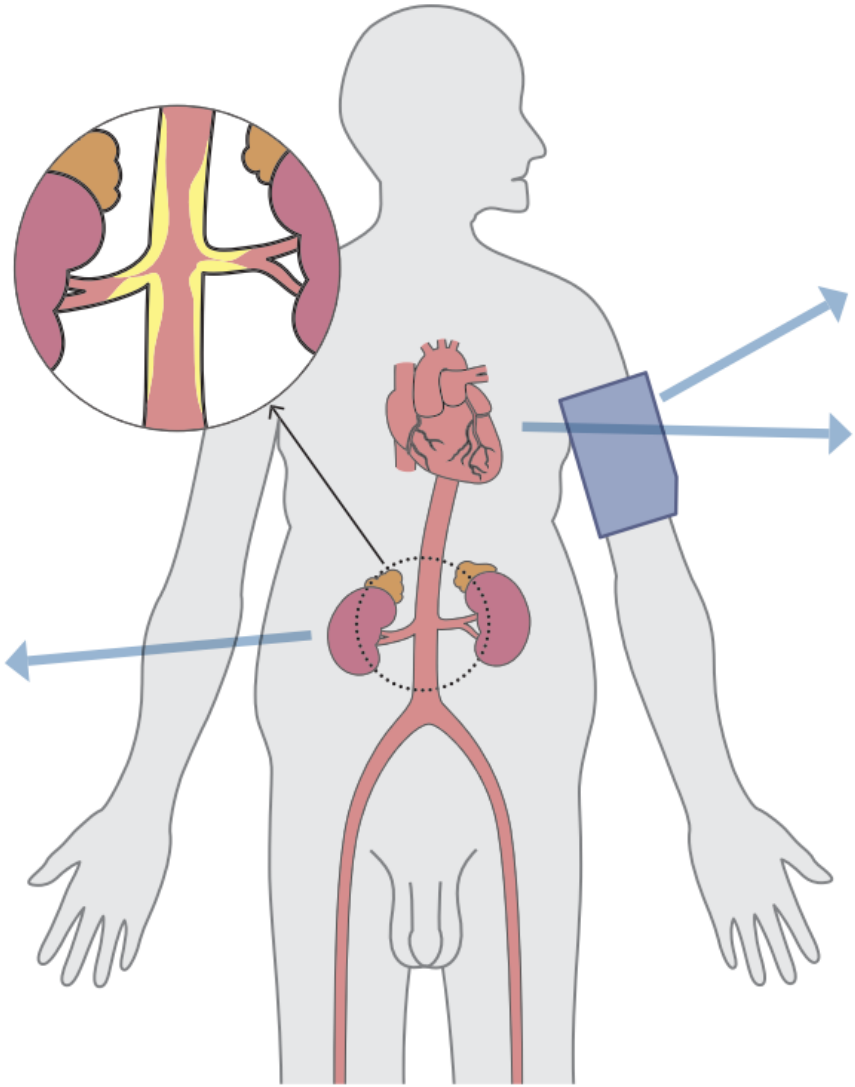
Renal artery duplex ultrasound; otherwise angio-CT or angio-MR

Further work-up

Angio-CT or angio-MR
Invasive catheter angiography

Treatment[c,d]

Antihypertensive treatment
Strict control of CV risk factors
Revascularization (selected cases)



Cardiovascular phenotype

24h ABPM – resistant hypertension, frequent non-dipping

- LVH
- Decreased diastolic function
- Decreased systolic function

Increased CV Risk and mortality

[a]The prevalence of ARVD differs considerably between studied populations – in a population-based cohort >65 years of age, ARVD (defined as >60% stenosis) was identified in 6.8%. Among hypertensives, the prevalence of ARVD is probably around 1% in patients with mild hypertension, but may be as high as 14%–24% in patients with severe or resistant hypertension.

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Ινομυώδης Δυσπλασία - Νεφραγγειακή Νόσος

Prevalence:
<1 to 6%[a]

Suggestive symptoms, signs and findings

Early-onset/ severe hypertension
Migraine
Pulsatile tinnitus

1st choice screening test[b]

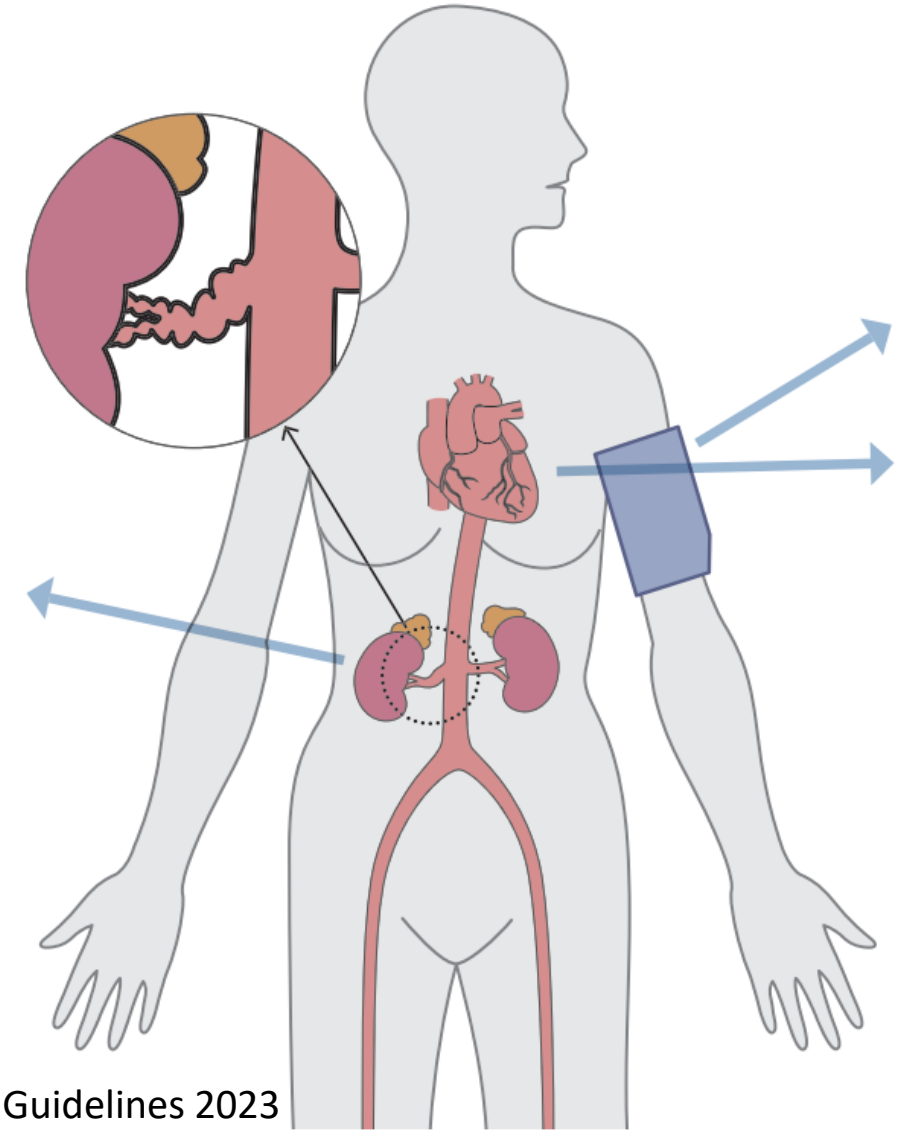
Renal artery duplex ultrasound; otherwise angio-CT or angio-MR

Treatment

Antihypertensive treatment
Angioplasty without stenting[c,d]

Follow-up

- Whole body angio-CT or angio-MR at diagnosis[e]
- Indefinite follow-up



Cardiovascular phenotype

24h ABPM – early onset or resistant hypertension

Frequent in patients with Spontaneous Coronary Artery Dissection (SCAD)

May affect all medium sized arteries (most frequent: renal and cervical arteries)

Often associated with arterial dissections and aneurysms

Cardiovascular phenotype:
From asymptomatic to resistant hypertension, stroke, renal, mesenteric or myocardial infarction

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Νεφραγγειακή Νόσος

FIGURE 43-15 Computed tomography angiogram with three-dimensional reconstruction, showing a severe proximal atherosclerotic stenosis of the right renal artery **(A)** and the classic "string-of-beads" lesion of fibromuscular dysplasia (bilateral in this patient) **(B)**. *(Courtesy Dr. Bart Domatch, Radiology Department, University of Texas Southwestern Medical Center, Dallas.)*

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Πρωτογενής Αλδοστερονισμός

Prevalence:
6–20%[a]

Suggestive symptoms, signs and findings

Resistant hypertension
Grade 2 or 3 hypertension
Hypokalemia/Potassium in the low-normal range
Atrial fibrillation
OSA
Adrenal incidentaloma[b]
Family history of PA/early stroke

1st choice screening test[c]

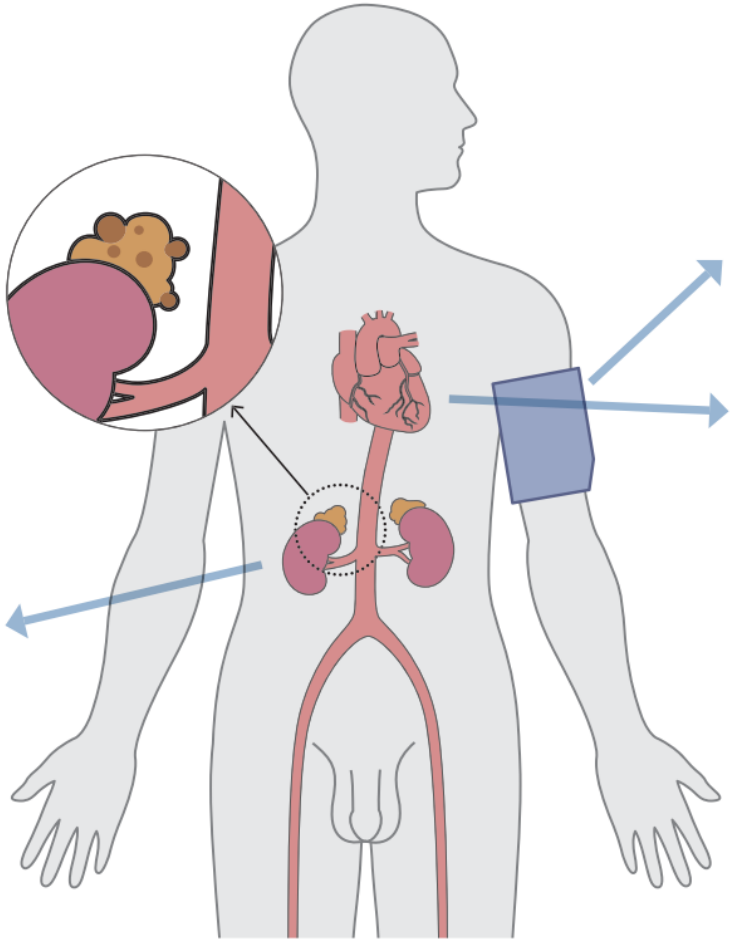
Plasma aldosterone to renin ratio (ARR)

Further work-up[d]

CT scanning
IV saline infusion test (SIT)
Fludrocortisone suppression test (FST)
Oral sodium loading test (SLT)
Captopril challenge test (CCT)
Adrenal vein sampling
Genetic testing in selected cases[e]

Treatment

Surgical treatment (laparoscopic adrenalectomy) – unilateral PA
Medical treatment – bilateral adrenal disease[f]



Cardiovascular phenotype

24 ABPM – true resistant hypertension, frequent non-dipping

- LVH
- Decreased diastolic function
- Myocardial fibrosis (MRI)

Increased CV Risk and mortality

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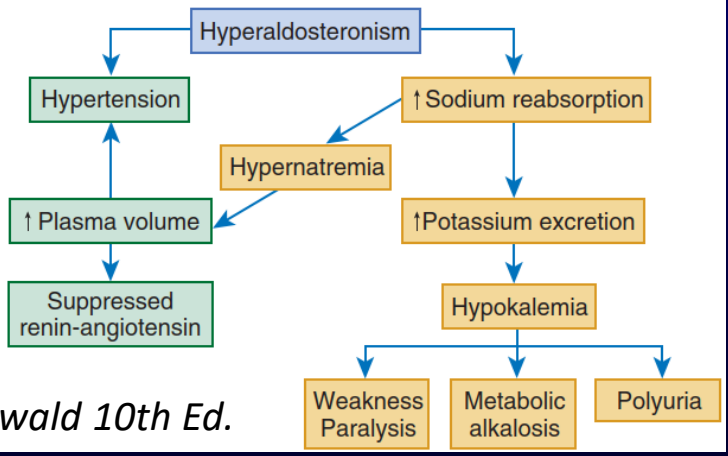
ΠΑΘΟΦΥΣΙΟΛΟΓΙΑ



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Φαιοχρωμοκύτωμα & Παραγαγγλίωμα

Prevalence:
<1%[a]

Suggestive symptoms and signs[b]

- paroxysmal symptoms (such as headache, sweating, palpitation, increased HR)
- large BP variation
- CV manifestations (e.g. MI, arrhythmias, Takotsubo cardiomyopathy)

1st choice screening test

Plasma or urinary free metanephrines

Further work-up

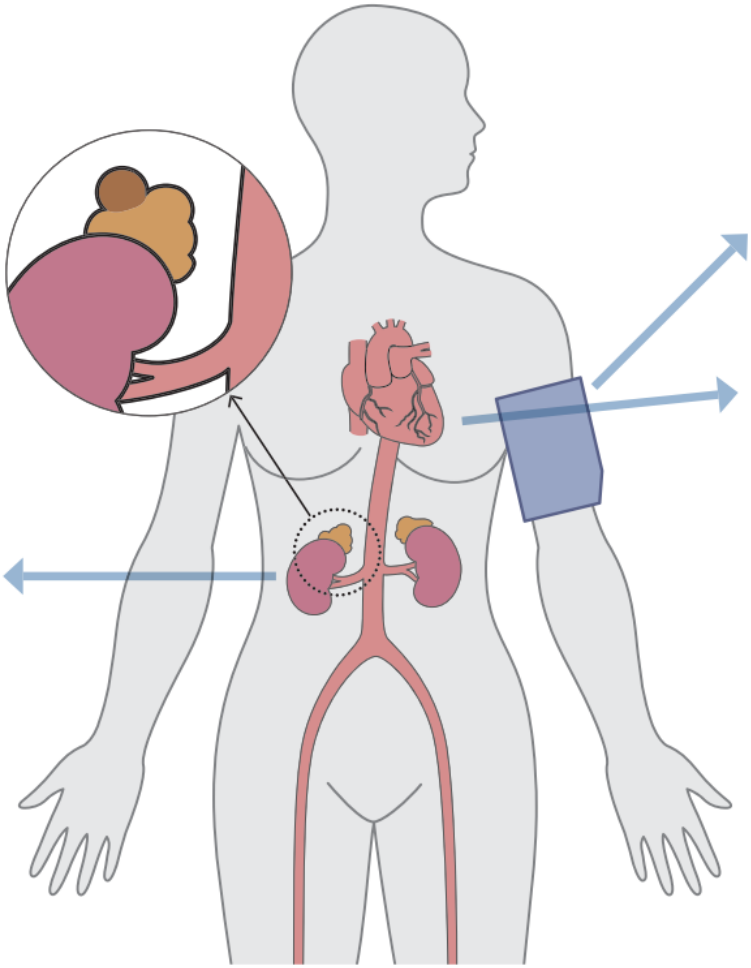
Contrast enchanced CT or MRI
Functional imaging
Genetic testing[c]

Treatment[d]

Surgical resection
(Pheochromocytoma: minimally invasive laparoscopic adrenalectomy)

Follow-up[e]

In most cases > 10 yrs



Cardiovascular phenotype

24h ABPM – frequent non-dipping

- LVH
- Decreased systolic function
- Myocardial fibrosis (MRI)

Increased CV Risk and mortality

Hypertension, Persistent or Paroxysmal
Markedly variable blood pressures (±orthostatic hypotension)
Sudden paroxysms (±subsequent hypertension) in relation to:
Stress: anesthesia, angiography, parturition
Pharmacologic provocation: histamine, nicotine, caffeine, beta blockers, glucocorticoids, tricyclic antidepressants
Manipulation of tumors: abdominal palpation, urination
Rare patients persistently normotensive
Unusual settings
Childhood, pregnancy, familial
Multiple endocrine adenomas: medullary carcinoma of the thyroid (MEN-2), mucosal neuromas (MEN-2B)
Von Hippel–Lindau syndrome
Neurocutaneous lesions: neurofibromatosis
Associated Symptoms
Sudden spells with headache, sweating, palpitations, nervousness, nausea, vomiting
Pain in chest or abdomen
Associated Signs
Sweating, tachycardia, arrhythmia, pallor, weight loss

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Σύνδρομο Cushing

Prevalence: 2–5%[a]

Suggestive symptoms and signs

Resistant hypertension
Easy bruising, facial plethora, ‚moon' face, skin thinning
Proximal myopathy
Weight gain with centripetal distribution of body fat
Diabetes mellitus

1st choice screening test[b]

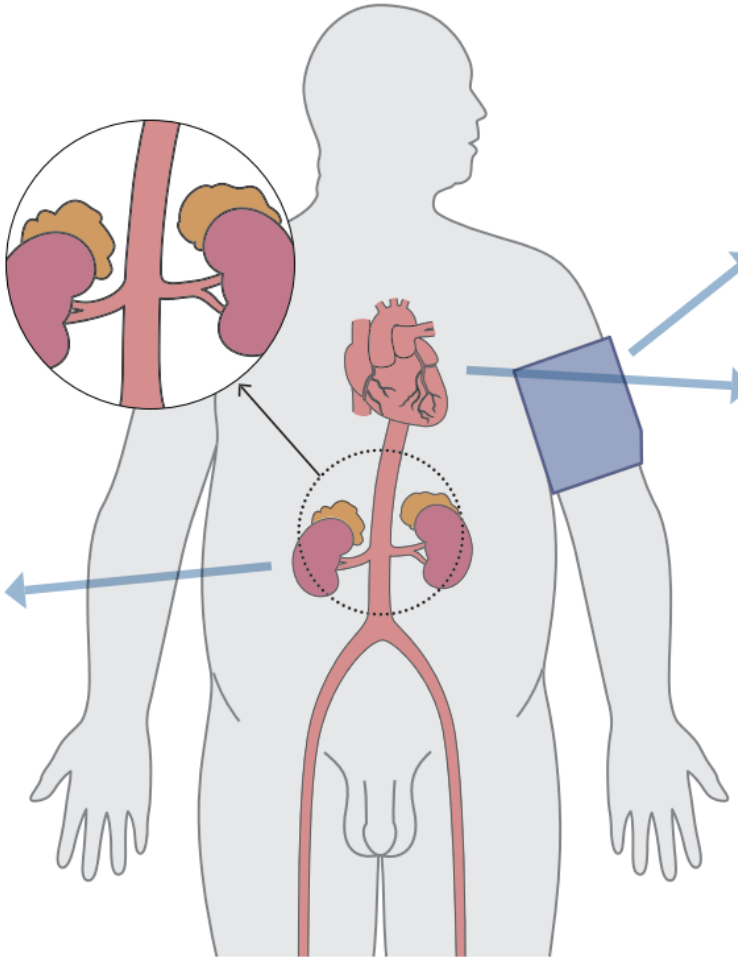
Overnight 1 mg dexamethasone suppression test
24-h urinary free cortisol
Late-night salivary cortisol

Further work-up

Morning plasma ACTH
ACTH stimulation by CRH or desmopressin
CT

Treatment

Medical – normalization of cortisol levels
Surgical – first line treatment for Cushing's disease , ectopic Cushing's syndrome and ACTH-independent hypercortisolism



Cardiovascular phenotype

24h ABPM – frequent non-dipping
Short-term BP variability

- LVH
- Decreased systolic function
- Decreased diastolic function

Increased CV Risk and mortality

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Σπάνια Γενετικά Αίτια 2παθούς ΑΥ

Condition	Phenotype	Mechanism and effect
Liddle syndrome	Hypokalaemia, metabolic alkalosis, low PRA or PRC, low PAC	Increased renal tubular ENaC activity: responds to treatment with amiloride
Apparent mineralocorticoid excess	Hypokalaemia, metabolic alkalosis, low PRA or PRC, low PAC	Decreased 11β-dehydrogenase isoenzyme 2
Gordon syndrome	Hyperkalaemia, metabolic acidosis, low PRA or PRC, low PAC	Overactivity of sodium chloride co-transporter
Geller syndrome	Pregnancy-exacerbated hypertension, low PRA or PRC, low PAC	Agonist effect of progesterone on the min-eralocorticoid receptor
Glucocorticoid remediable hypertension	Hypokalaemia, metabolic alkalosis, low PRC or PRA, and increased PAC	Chimeric CYP11β1 to CYP11β2 gene: response to treatment with glucocorticoids

ENaC = epithelial sodium channel; PAC = plasma aldosterone concentration; PRA = plasma renin activity; PRC = plasma renin concentration.

Φάρμακα ως αίτιο για 2παθή ΑΥ

Medication/substance	
Oral contraceptive pill	Especially oestrogen containing; cause hypertension in ~5% of women, usually mild but can be severe
Diet pills	For example, phenylpropanolamine and sibutramine
Nasal decongestants	For example, phenylephrine hydrochloride and naphazoline hydrochloride
Stimulant drugs	Amphetamine, cocaine, and ecstasy; these substances usually cause acute rather than chronic hypertension
Liquorice	Chronic excessive liquorice use mimics hyperaldosteronism by stimulating the mineralocorticoid receptor and inhibiting cortisol metabolism
Immunosuppressive medications	For example, cyclosporin A (tacrolimus has less effect on BP and rapamycin has almost no effect on BP) and steroids (e.g. corticosteroids and hydrocortisone)
Antiangiogenic cancer therapies	Antiangiogenic drugs such as VEGF inhibitors (e.g. bevacizumab), tyrosine kinase inhibitors (e.g. sunitinib), and sorafenib have been reported to increase BP
Other drugs and substances that may raise BP	Anabolic steroids, erythropoietin, non-steroidal anti-inflammatory drugs, and herbal remedies (e.g. ephedra and ma huang)

BP = blood pressure; VEGF = vascular endothelial growth factor.

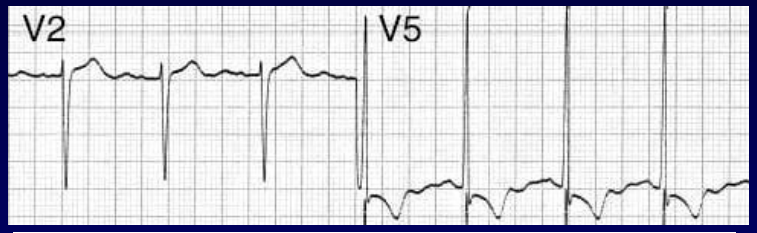
Βλάβη οργάνων στόχων

- Καρδιά
  - LVH
  - Στηθάγχη-έμφραγμα
  - Καρδιακή ανεπάρκεια
- Εγκέφαλος
  - ΑΕΕ
- ΧΝΑ
- Περιφερική αρτηριακή νόσος
- Αμφιβληστροειδοπάθεια

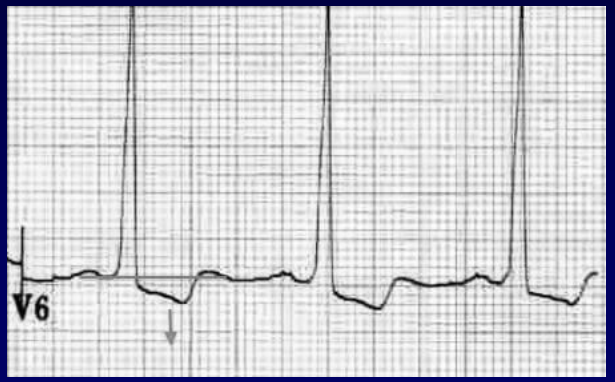
Κριτήρια για τον καθορισμό βλάβης οργάνων στόχων

Measurement	Parameter	Abnormality threshold
ECG		
LVH	$S_{V1} + R_{V5}$ (Sokolow–Lyon)	>35 mm
	R wave aVL	≥11 mm
LVH	$S_{V3} + R_{aVL}$ (Cornell voltage) Cornell voltage (+6 mm in W) × QRS duration (Cornell duration product)	>28 mm (M), >20 mm (W) >2440 mm s
ECHO		
LVH	LVM/BSA (g/m^2)	>115 (M), >95 (W)
	LVM/height ($g/m^{2.7}$)	>50 (M), >47 (W)
RWT	LV conc. Remodeling	≥0.43
LV chamber size	LVDDiam/height	>3.4 (M), >3.3 (W) cm/m
LV diastolic dysfunction	*e′* velocity septal	<7 cm/s
	e′ velocity lateral	<10 cm/s
LV filling pressure	*E*/*e′* average ratio	>14
	LAV/BSA	>34 ml/m^2
	LAV/$height^2$	>18.5 (M) or >16.5 (W) ml/m^2
LV systolic dysfunction	GLS	<20%
Kidney		
Function	eGFR	<60 $ml/min/1.73\,m^2$
Albuminuria	UACR	>30 mg/g
Renal resistive index	RRI	>0.7
Large artery stiffness		
Pulse pressure	Brachial PP (>60 years)	≥60 mmHg
Pulse wave velocity	baPWV (in people 60–70 years)	>18 m/s
	cfPWV (in people 50–60 years)	>10 m/s
Carotid atherosclerosis		
	Plaque	IMT ≥1.5 mm, or focal increase in thickness ≥0.5 mm, or 50% of surrounding IMT
	IMT	>0.9 mm
Coronary atherosclerosis		
	CAC	Age-specific and sex-specific reference value
LEAD		
	ABI	<0.9
Eye		
	KWB score	Grade III (hemorrhages, microaneurysms, hard exudates and cotton wool spots) and grade IV (papilledema and/or macula edema)
Microvascular changes	Wall-to-lumen ratio	no established reference value

ΗΚΓ: Υπερτροφία ΑΡ κοιλίας (LVH)

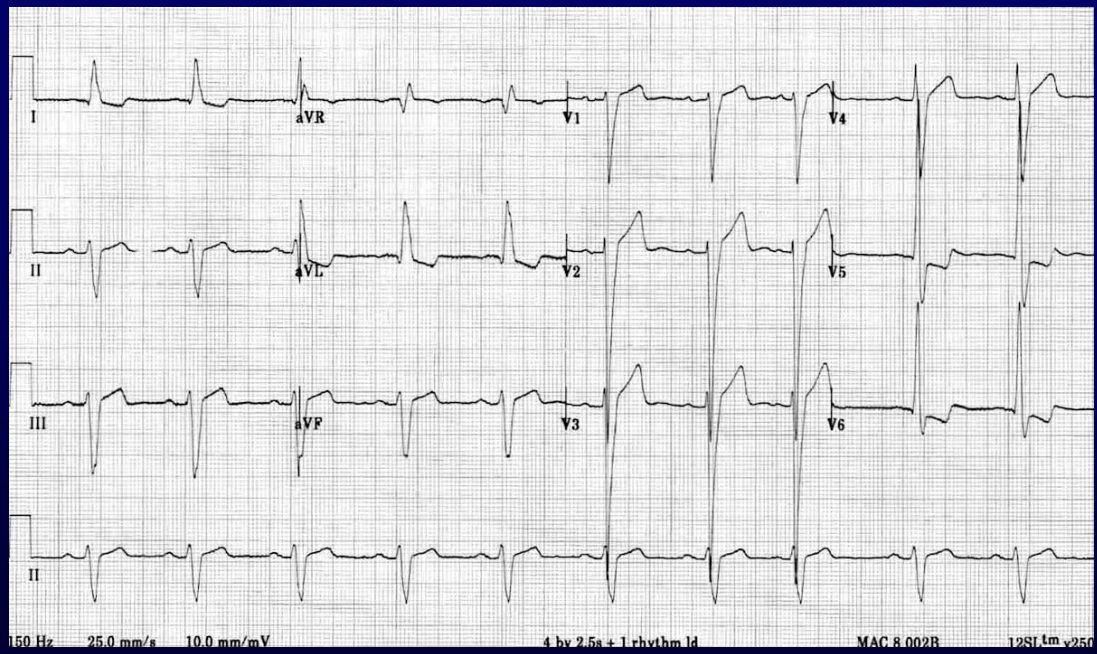


LVH by voltage criteria: S wave in V2 + R wave in V5 > 35 mm

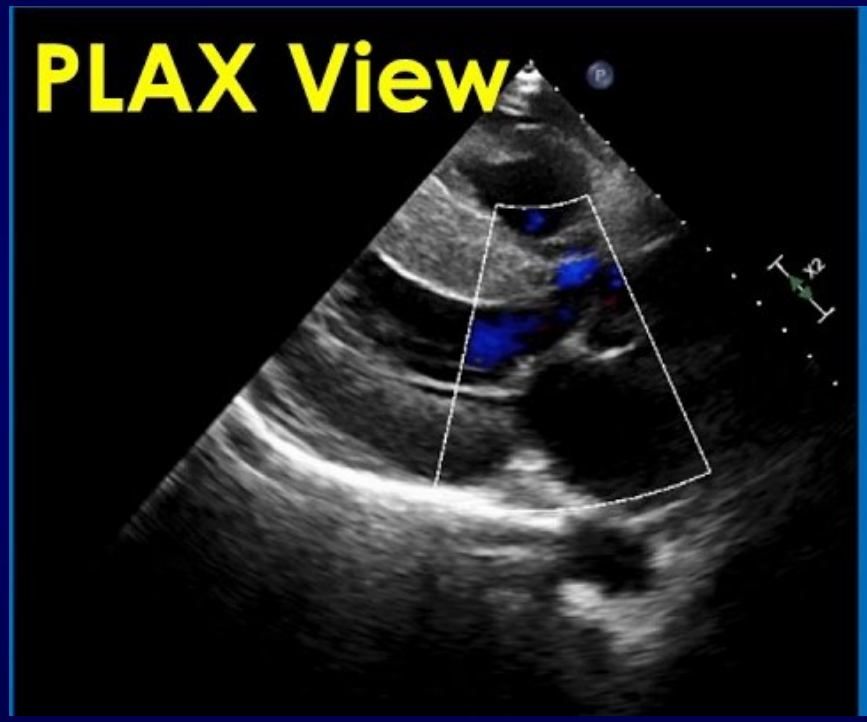


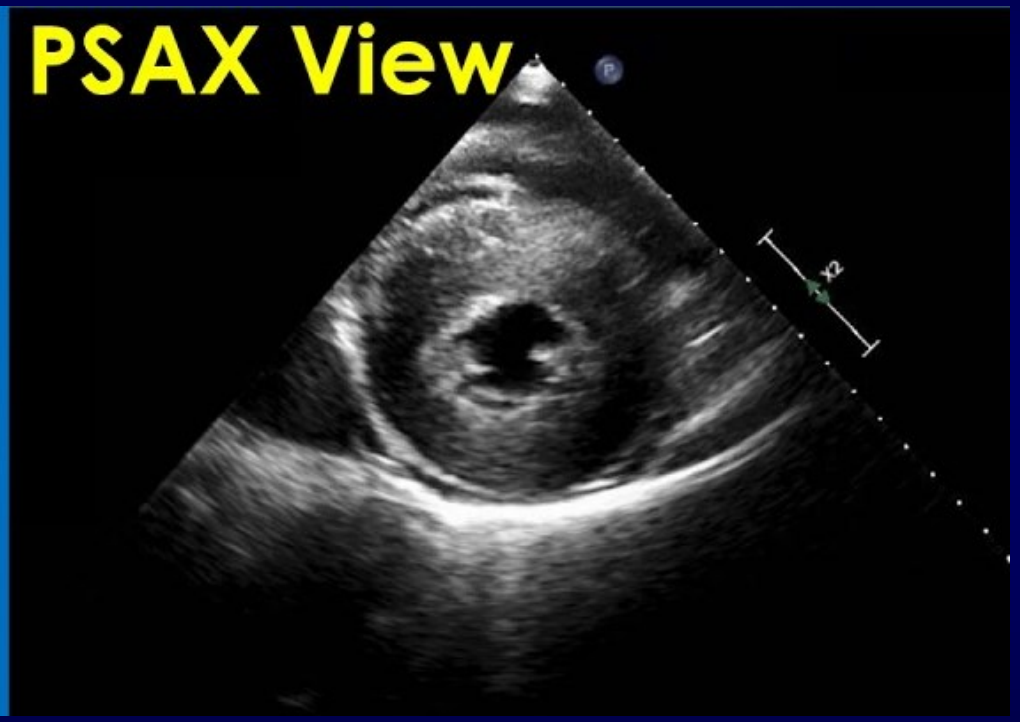
LV strain pattern: ST depression and T wave inversion in the lateral leads

- **Markedly increased LV voltages:** huge precordial R and S waves that overlap with the adjacent leads (SV2 + RV6 >> 35 mm)
- R-wave peak time > 50 ms in V5-6 with associated QRS broadening
- **LV strain pattern** with ST depression and T-wave inversions in I, aVL and V5-6
- Prominent U waves in V1-3
- Left axis deviation

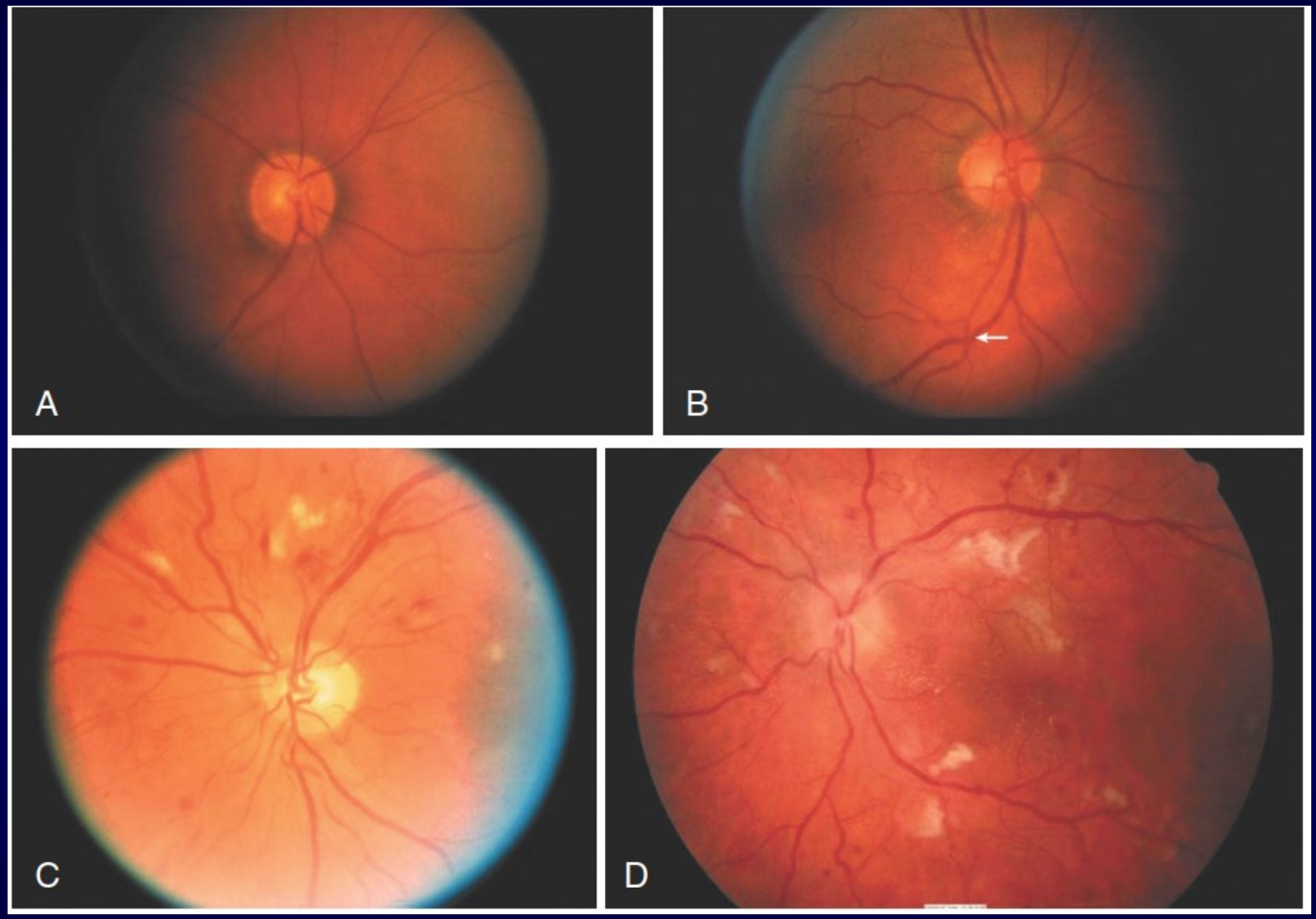


Echo: Υπερτροφία ΑΡ κοιλίας





Στάδια Υπερτασικής Αμφιβληστροειδοπάθειας



Retinal photographs showing the stages of hypertension retinopathy. A. Mild diffuse arteriolar narrowing. B. Arterial-venous nicking. C. Hemorrhages and exudates. D. Papilledema.

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Αρχικός Εργαστηριακός Έλεγχος

- Hemoglobin and/or hematocrit
- Fasting blood glucose and HbA1c
- Blood lipids: total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides
- Blood potassium and sodium
- Blood uric acid
- Blood creatinine (and/or cystatin C) for estimating GFR with eGFRa formulas
- Blood calcium
- Urine analysis (first voided urine in the morning), multicomponent dipstick test in all patients, urinary albumin/creatinine ratio, microscopic examination in selected patients

Παρακλινικός Έλεγχος: Τυπικός και Εκτεταμένος

Basic screening tests for HMOD recommended for all hypertensive patients	Aim
12 lead ECG	Measure HR and AV conduction, detect cardiac arrhythmias, myocardial ischemia and infarction, screen for LVH
Urine albumin : creatinine ratio (UACR)	Detect and classify CKD
Serum creatinine and eGFR	Detect and classify CKD
Extended screening for HMOD	
Echocardiography	Evaluate structure and function of the ventricles and left atrium, detect valvular disease, aortic root diameter and ascending aortic aneurysm
cfPWV or baPWV	Evaluate aortic/large artery stiffness
Carotid artery ultrasound	Determine carotid intima-media thickness, plaque and stenosis
Coronary artery calcium scan	Determine the presence and extent of coronary calcium to predict CAD events
Abdominal aorta ultrasound	Screen for aortic aneurysm
Kidney ultrasound	Evaluate size and structure of kidney, detect renovascular disease, determine RRI (by spectral doppler ultrasonography)
Spectral doppler ultrasonography	Diagnosis of renovascular disease and determination of RRI
ABI	Screen for LEAD
Retina microvasculature	Detect microvascular changes
Cognitive function testing (MMSE, MoCA)	Screen for early stages of dementia
Brain imaging (CT, MRI)	Detect structural brain damage

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Κλινική Εκτίμηση Βλάβης Οργάνων Στόχων

Clinical evaluation and HMOD assessment

Recommendations	Class[a]	Level[b]
Heart		
12-lead ECG is recommended for all hypertensive patients.[120]	I	B
Echocardiography: • Is recommended in hypertensive patients when there are ECG abnormalities or signs or symptoms of LV dysfunction.[42,134]	I	B
• May be considered when the detection of LVH may influence treatment decisions.[42,134]	IIb	B
Blood vessels		
Ultrasound examination of the carotid arteries:	I	B
• May be considered for the detection of asymptomatic atherosclerotic plaques or carotid stenosis in patients with documented vascular disease elsewhere.[42]	IIb	B
Measurement of PWV may be considered for measuring arterial stiffness.[109,189]	IIb	B
Measurement of ABI may be considered for the detection of advanced LEAD.[153,190]	IIb	B
Kidney		
Measurement of serum creatinine and eGFR is recommended in all hypertensive patients.[180]	I	B
Measurement of urine albumin:creatinine ratio is recommended in all hypertensive patients.[43,180]	I	B
Renal ultrasound and Doppler examination should be considered in patients with impaired renal function, albuminuria, or for suspected secondary hypertension.	IIa	C
Fundoscopy		
Is recommended in patients with grades 2 or 3 hypertension and all hypertensive patients with diabetes.	I	C
May be considered in other hypertensive patients.	IIb	C
Brain		
In hypertensive patients with neurological symptoms and/or cognitive decline, brain MRI or CT should be considered for detecting brain infarctions, microbleeds, and white matter lesions.[168,169]	IIa	B

ABI = ankle–brachial index; CT = computed tomography; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; HMOD = hypertension-mediated organ damage; LEAD = lower extremity arterial disease; LV = left ventricular; LVH = left ventricular hypertrophy; MRI = magnetic resonance imaging; PWV = pulse wave velocity; TIA = transient ischaemic attack.

[a]Class of recommendation.

[b]Level of evidence.

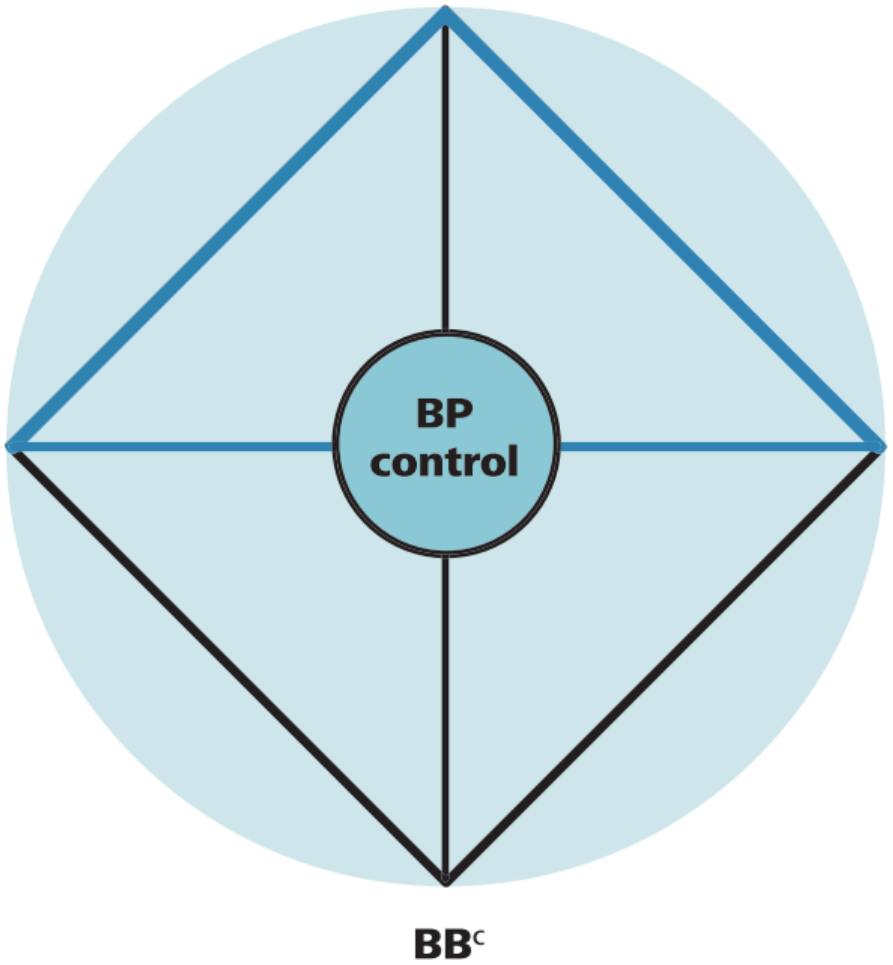
ESC Guidelines. Hypertension 2018

ФАРМАКА

Κατηγορίες Φαρμάκων

Prescribing patterns:

- Start with dual combination therapy in most patients
- Uptitrate to maximum well tolerated doses and to triple therapy if needed
- **Once daily (preferred in the morning)**
- **Add further drugs if needed**
- **Preferred use of SPCs at any step**



Additional drug classes

General antihypertensive therapy:

- Steroidal MRA
- Loop Diuretic
- Alpha-1 Blocker
- Centrally acting agent
- Vasodilator

Special comorbidities:

- ARNi
- SGLT2i
- Non-Steroidal MRA

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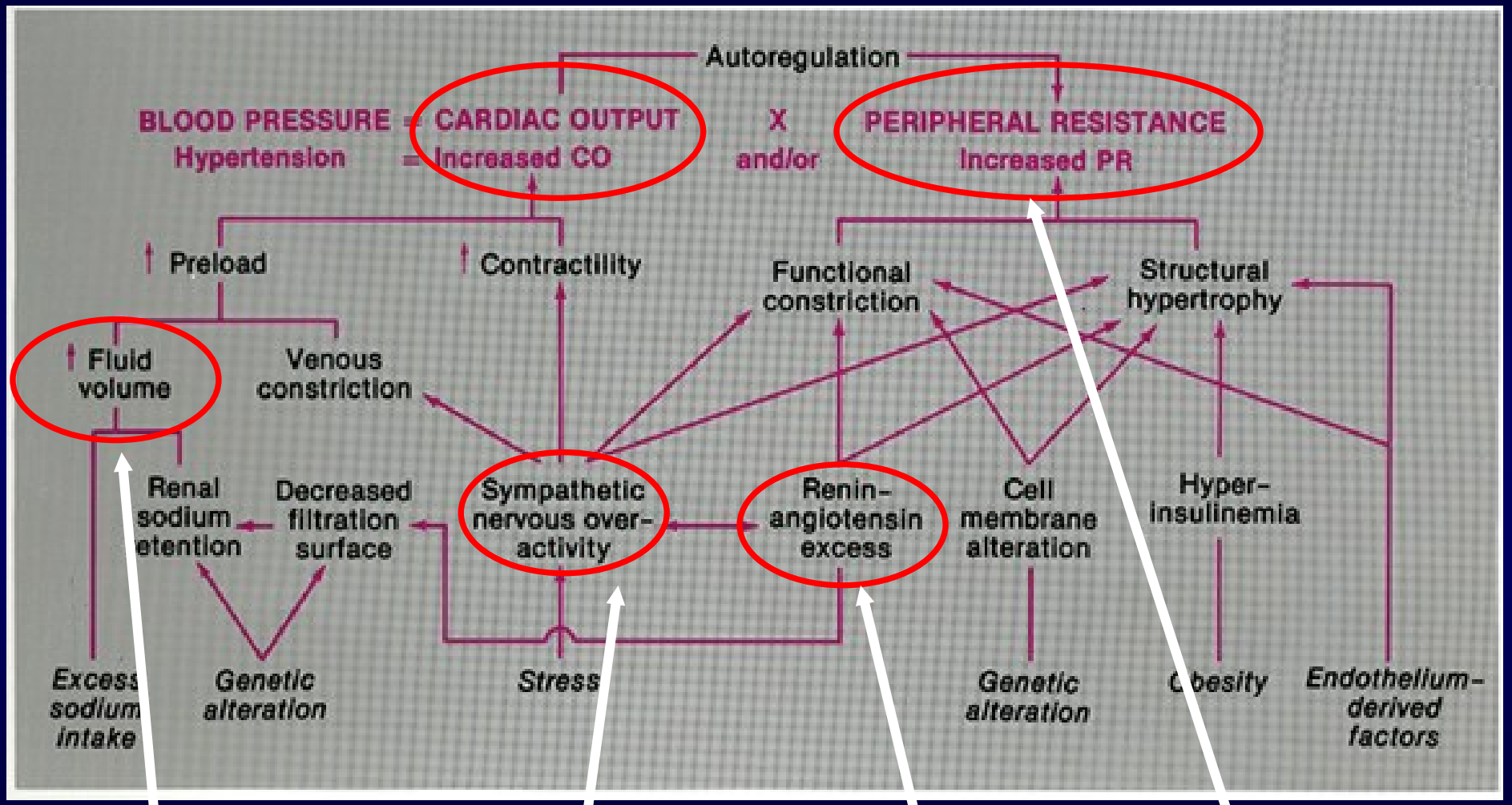
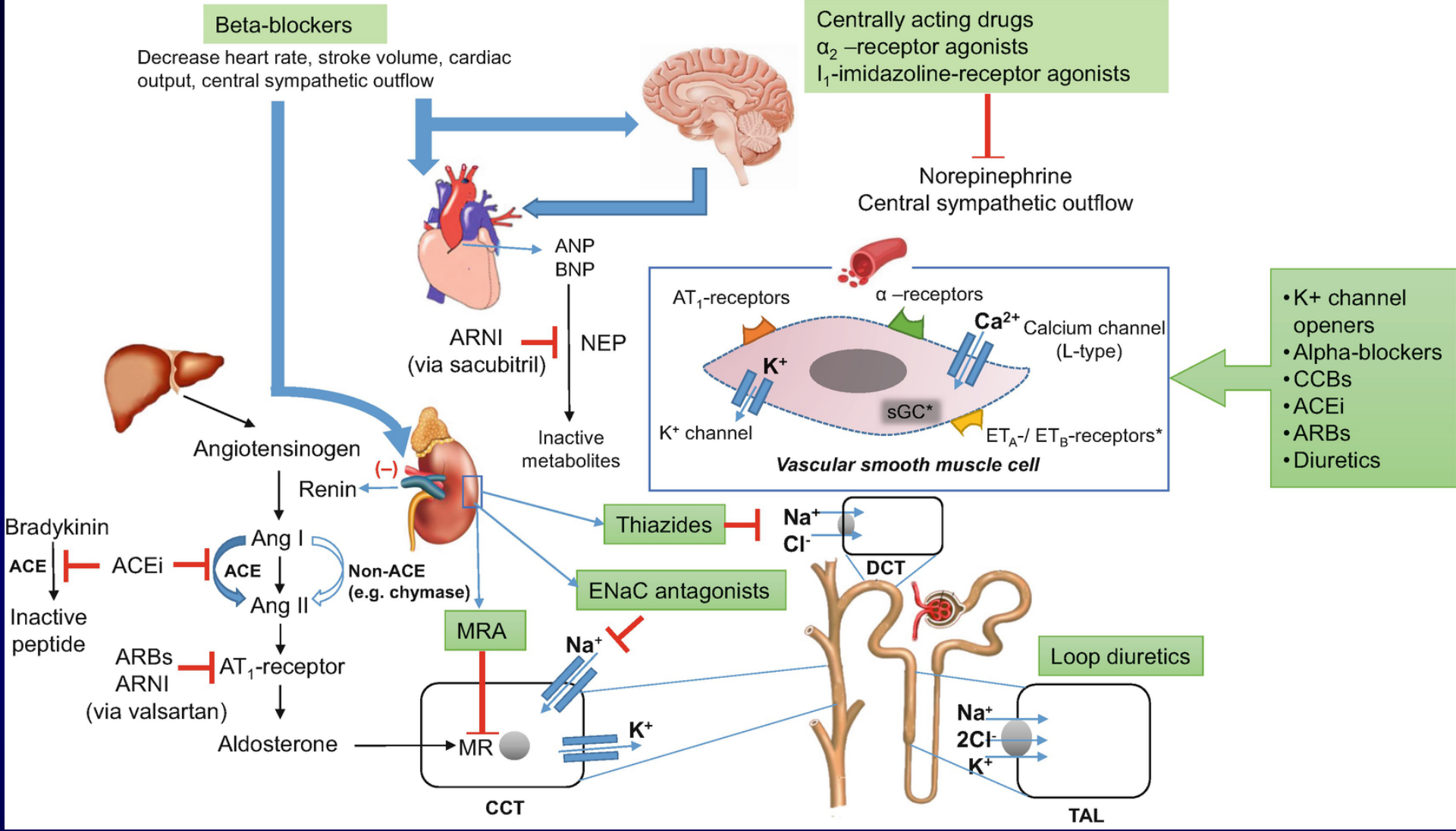
Αντι-υπερτασικά Φάρμακα

- Διουρητικά: Θειαζίδες,ινδαπαμίδη,χλωρθαλιδόνη, αγκύλης, Κ-συντηρητικά
- β-αποκλειστές: Μετοπρολόλη, Ατενολόλη, κτλ
- ACE-I/ARBs: Καπτοπρίλη, Ραμιπρίλη, Λισινοπρίλη, Ιρμπεσαρτάνη, Τελμισαρτάνη, κτλ
- CCBs: ΜΗ-Διυδροπυριδίνες (Βεραπαμίλη, Διλτιαζέμη), Διϋδροπυριδίνες (αμλοδιπίνη, λεκαρνιδιπίνη)
- Άμεσα δρώντα αγγειοδιασταλτικά: Υδραλαζίνη, μινοξιδίλη
- α+β-αποκλειστές: Λαβεταλόλη, Καρβεντιλόλη
- Κεντρικώς δρώντα: Μεθυλντόπα, Κλονιδίνη

BP = CO x PVR

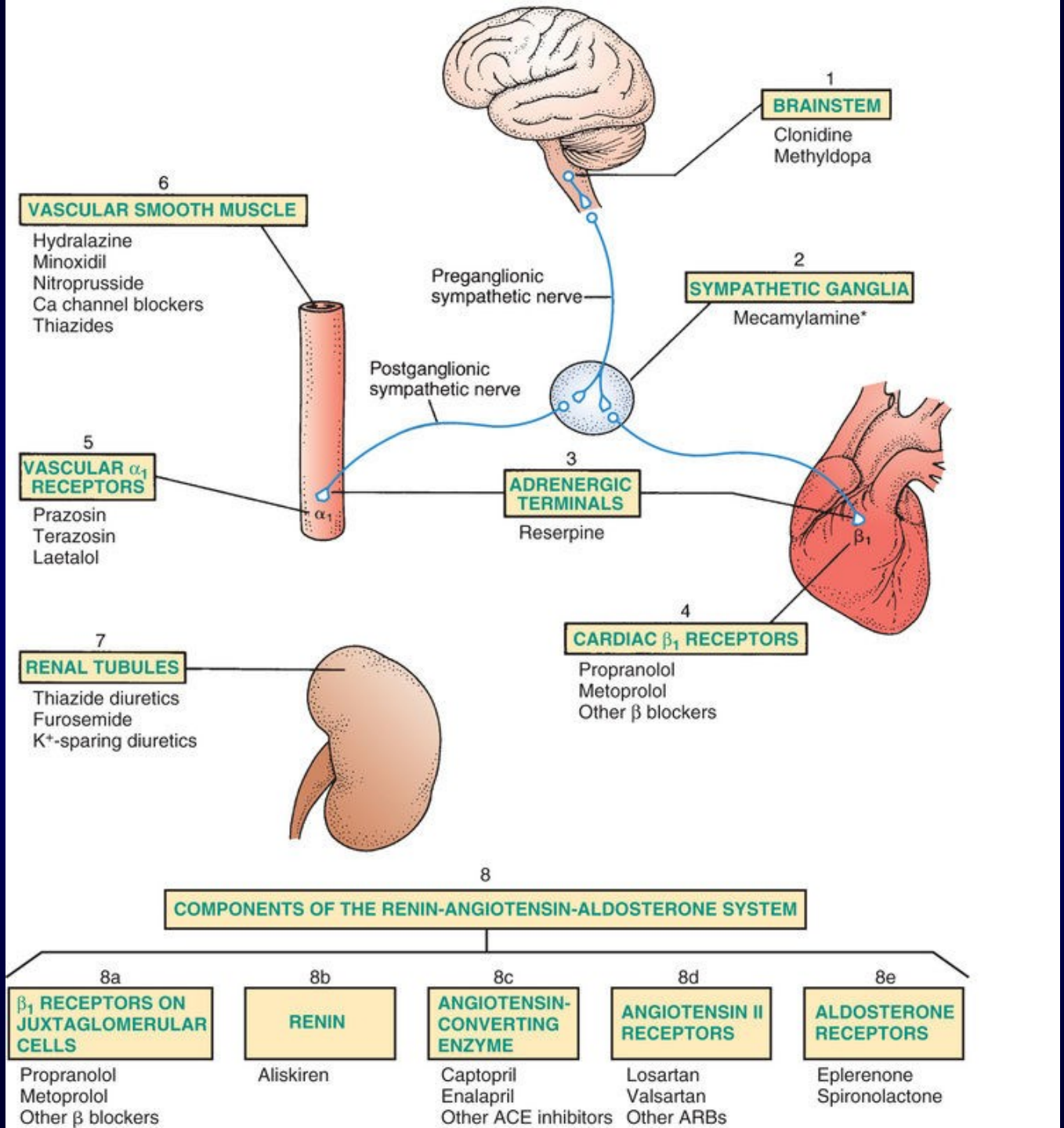


Διουρητικά Β-αποκλειστές ACE-I/ARBs CCBs/αγγειο-διασταλτικά



Site of action of different classes of antihypertensive drugs. Antihypertensive drugs are directed against a variety of pharmacological targets in various cell types in different organs involved in blood pressure control. The most important targets in the brain, heart, vasculature (vascular smooth muscle cells), and the kidney (nephron) are shown. Non-ACE-dependent conversion of angiotensin I (Ang I) to angiotensin II (Ang II) may occur independent from ACE due to the activity of other enzymes in different tissues such as chymase in the heart; (–) indicates inhibition. ACEi ACE inhibitors, ANP atrial natriuretic peptide, ARB angiotensin receptor blocker, ARNI angiotensin receptor–neprilysin inhibitor, BNP B-type natriuretic peptide, CCBs, calcium channel blockers, CCT cortical collecting duct, DCT distal convoluted tubule, ENaC epithelial sodium channel, MR mineralocorticoid receptor, MRA mineralocorticoid receptor antagonist, NEP neprilysin, TAL thick ascending limb of the loop of Henle, sGC soluble guanylate cyclase. ∗Indicates targets for novel antihypertensive drug development

https://link.springer.com/referenceworkentry/10.1007/978-3-030-57401-7_11


1
BRAINSTEM
Clonidine
Methyldopa
2
SYMPATHETIC GANGLIA
Mecamylamine*
Preganglionic sympathetic nerve
Postganglionic sympathetic nerve
3
ADRENERGIC TERMINALS
Reserpine
4
CARDIAC β_1 RECEPTORS
Propranolol
Metoprolol
Other β blockers
5
VASCULAR α_1 RECEPTORS
Prazosin
Terazosin
Laetalol
6
VASCULAR SMOOTH MUSCLE
Hydralazine
Minoxidil
Nitroprusside
Ca channel blockers
Thiazides
7
RENAL TUBULES
Thiazide diuretics
Furosemide
K+-sparing diuretics
8
COMPONENTS OF THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM
8a
β_1 RECEPTORS ON JUXTAGLOMERULAR CELLS
Propranolol
Metoprolol
Other β blockers
8b
RENIN
Aliskiren
8c
ANGIOTENSIN-CONVERTING ENZYME
Captopril
Enalapril
Other ACE inhibitors
8d
ANGIOTENSIN II RECEPTORS
Losartan
Valsartan
Other ARBs
8e
ALDOSTERONE RECEPTORS
Eplerenone
Spironolactone

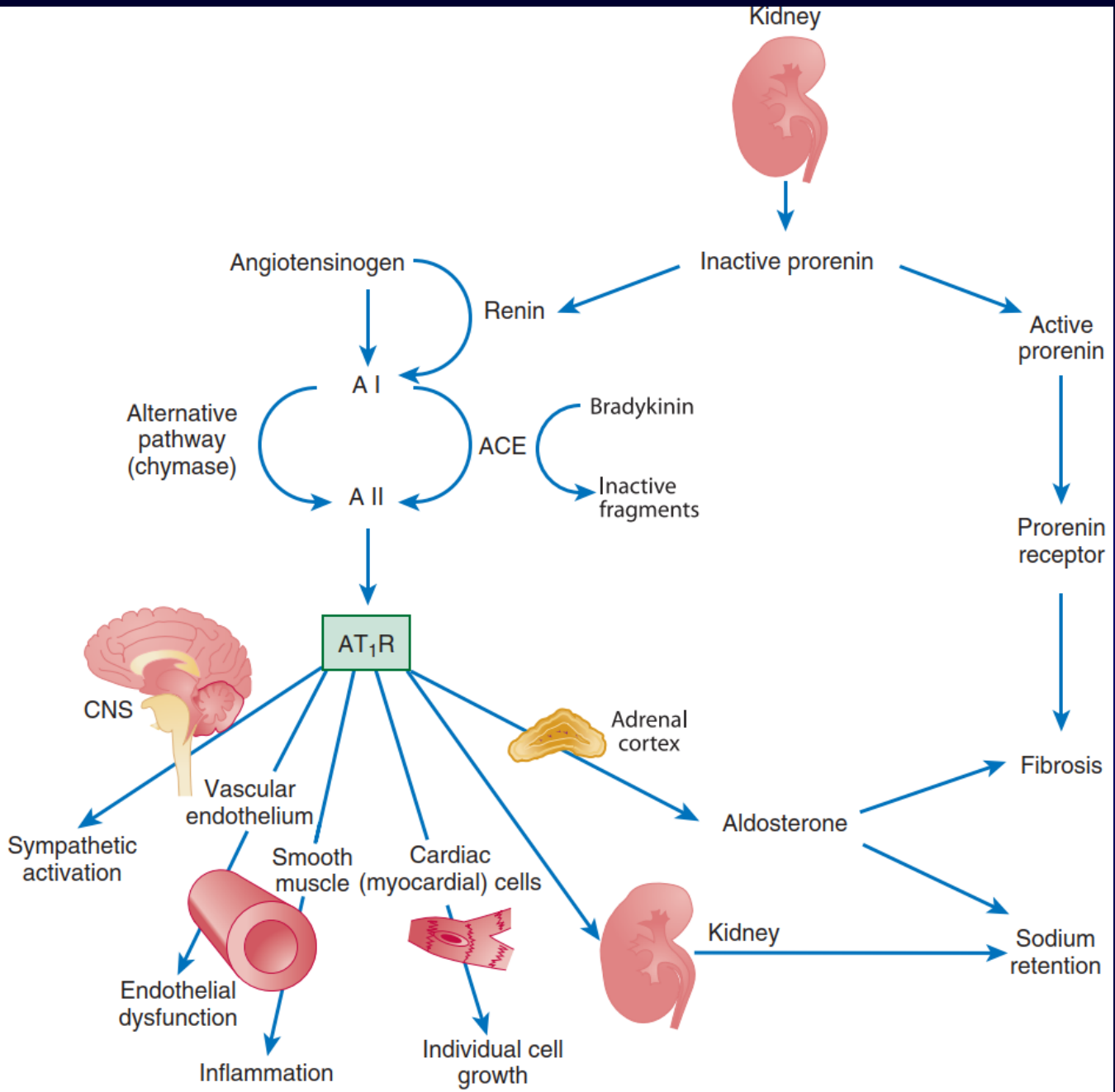
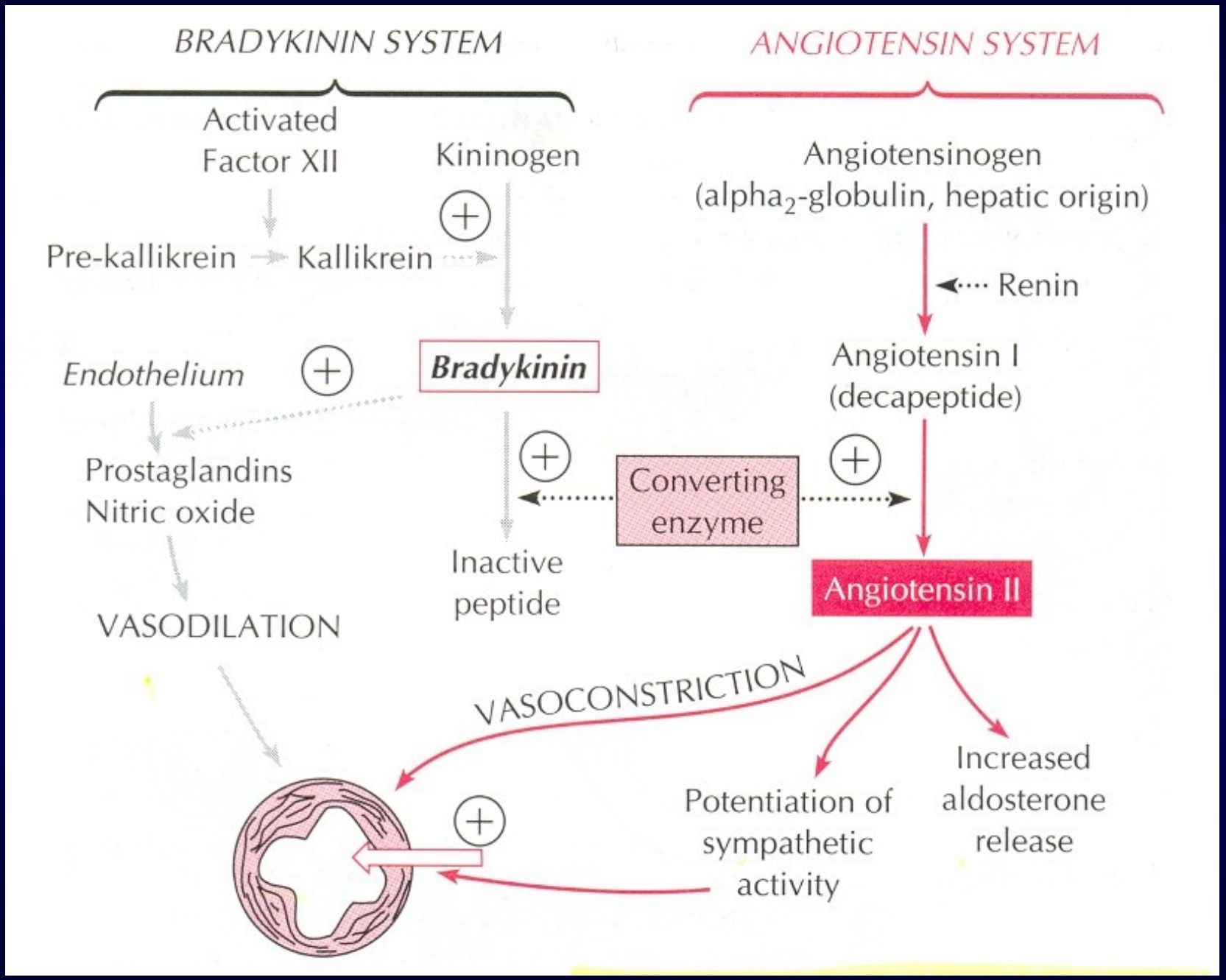
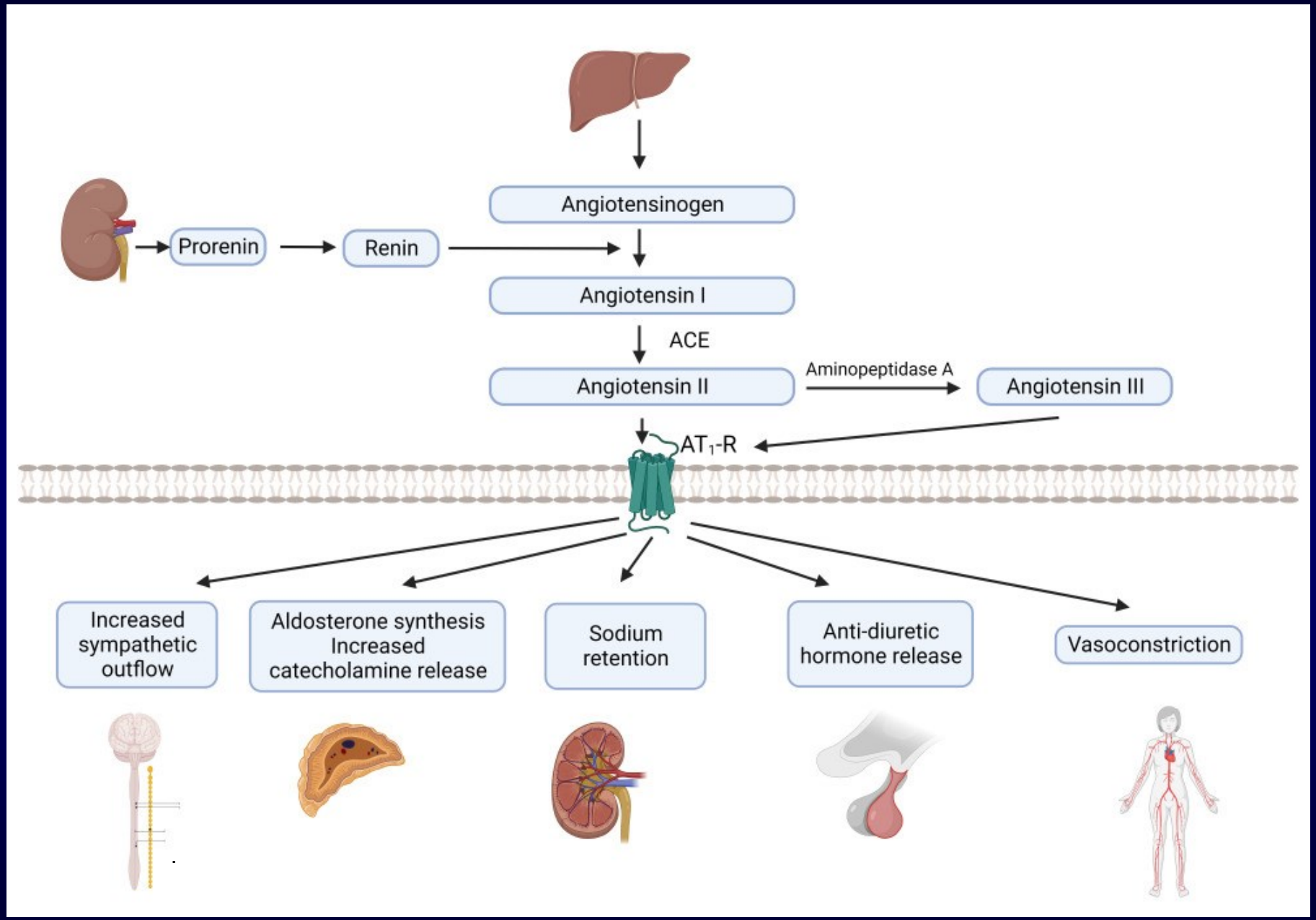
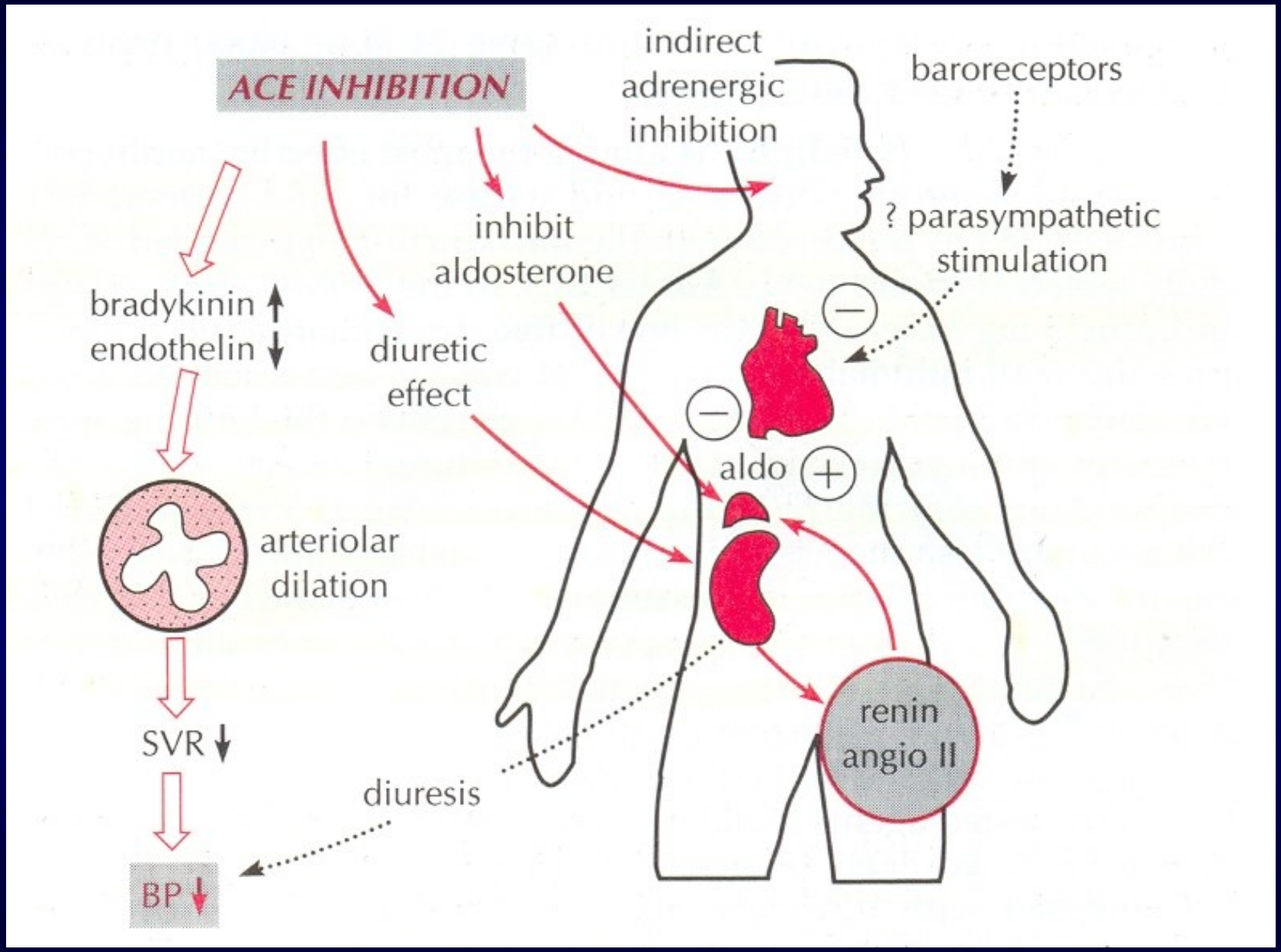


FIGURE 43-10 The renin-angiotensin-aldosterone system. AT_1R = angiotensin receptor type 1; CNS = central nervous system.

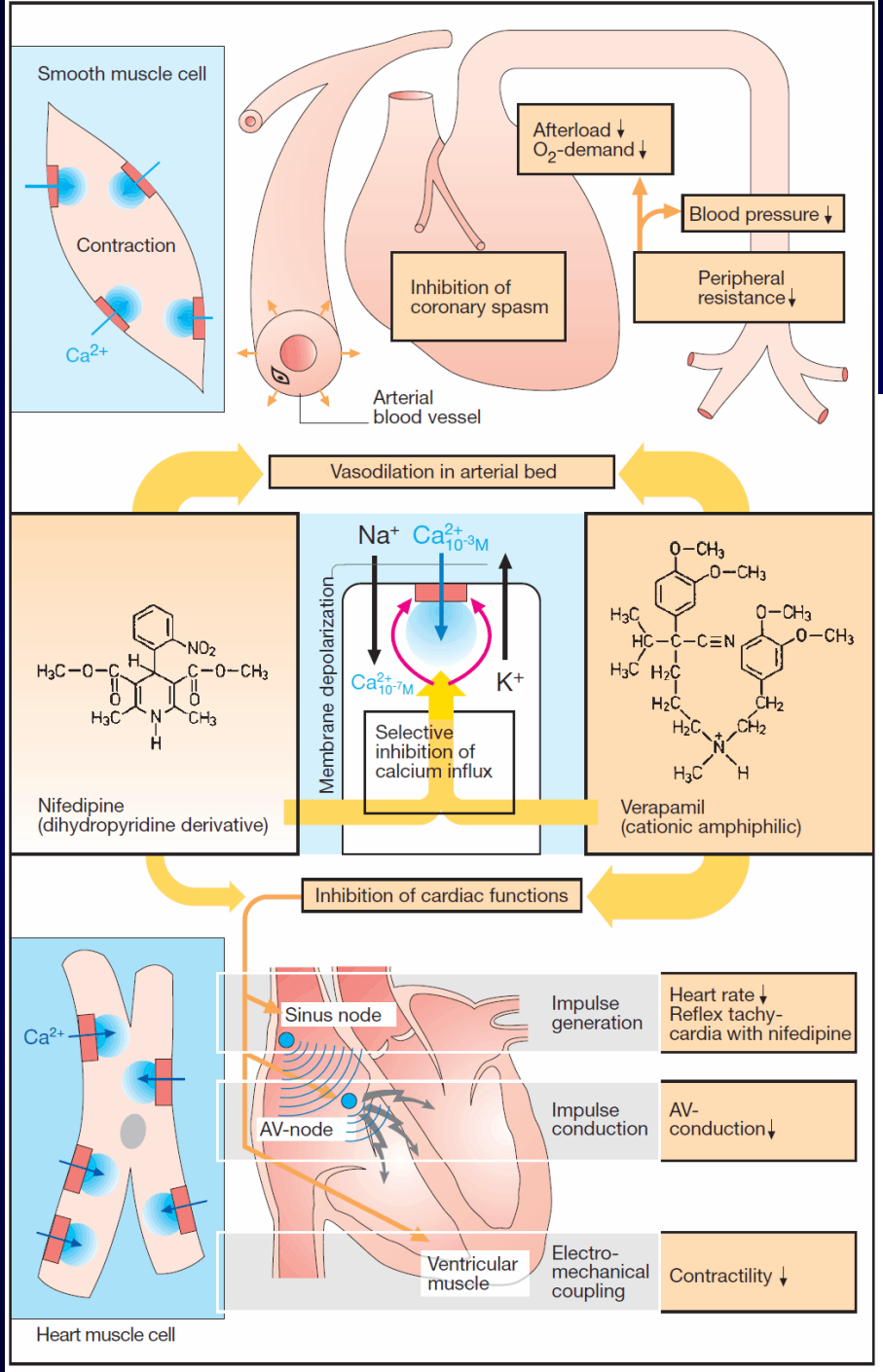

BRADYKININ SYSTEM
ANGIOTENSIN SYSTEM
Activated Factor XII
Kininogen
Angiotensinogen (alpha2-globulin, hepatic origin)
Pre-kallikrein
Kallikrein
Renin
Endothelium
Bradykinin
Angiotensin I (decapeptide)
Prostaglandins
Nitric oxide
Converting enzyme
Inactive peptide
Angiotensin II
VASODILATION
VASOCONSTRICTION
Potentiation of sympathetic activity
Increased aldosterone release

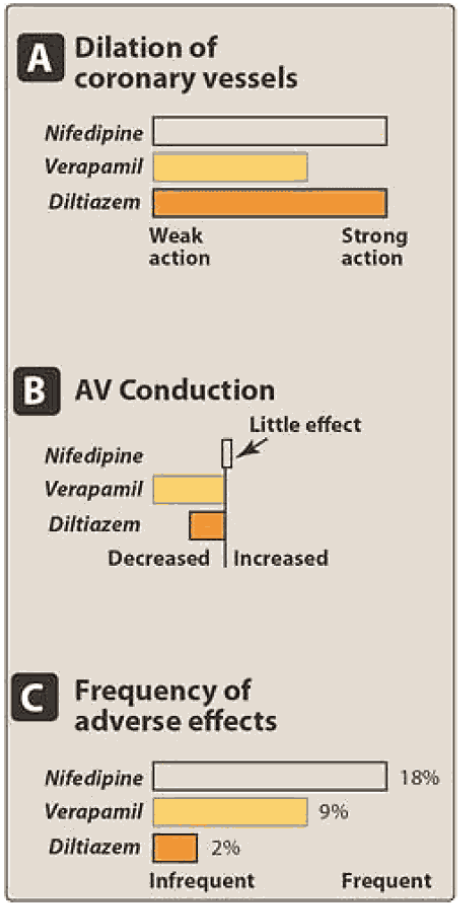


Physiology, Renin Angiotensin System
John H. Fountain; Jasleen Kaur; Sarah L. Lappin


ACE INHIBITION
indirect
adrenergic
inhibition
baroreceptors
? parasympathetic
stimulation
inhibit
aldosterone
bradykinin ↑
endothelin ↓
diuretic
effect
aldo
arteriolar
dilation
SVR ↓
renin
angio II
diuresis
BP ↓

Αποκλειστές Διαύλων Ασβεστίου

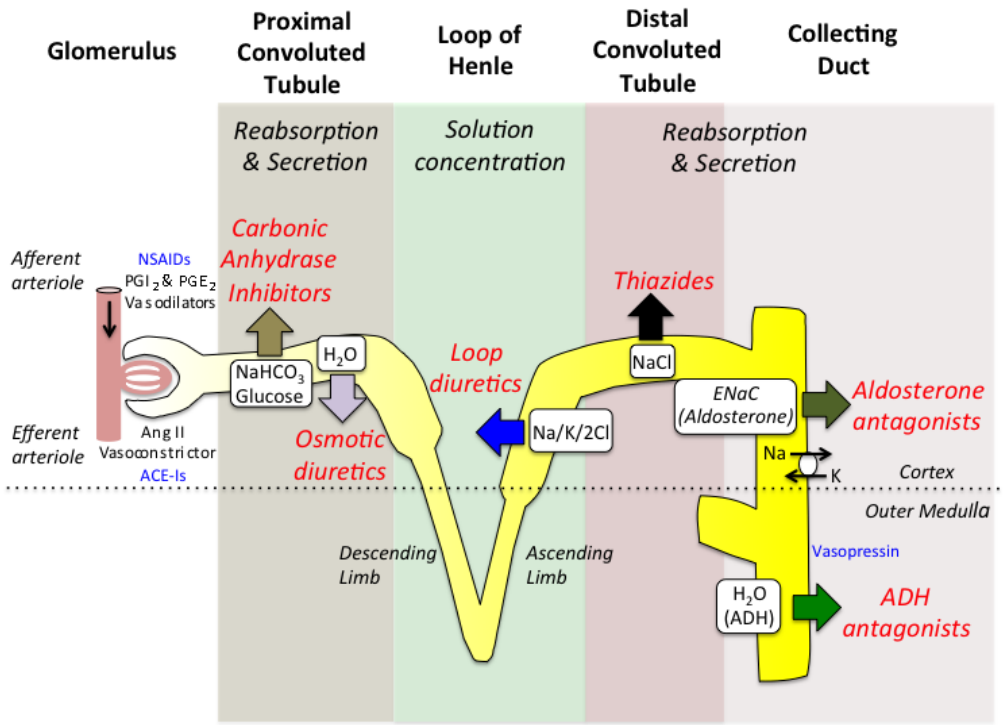


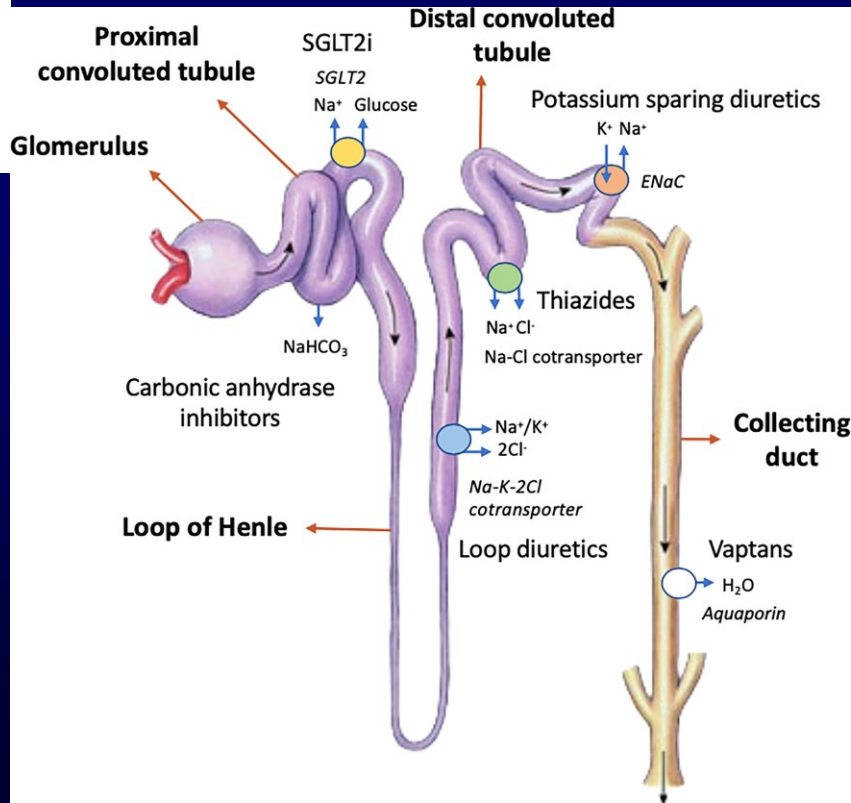


Actions of calcium-channel blockers.

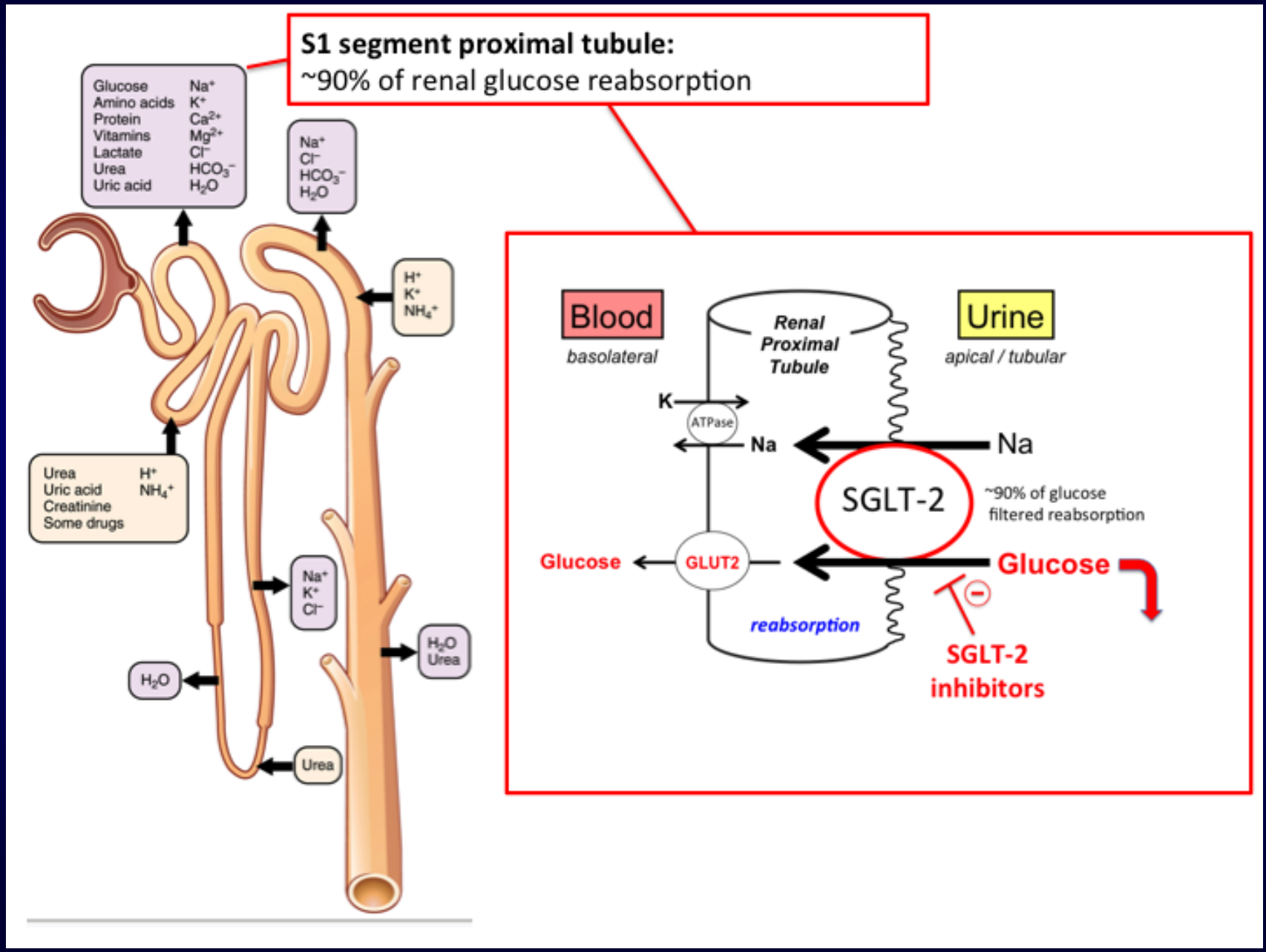
Vasodilators: calcium antagonists

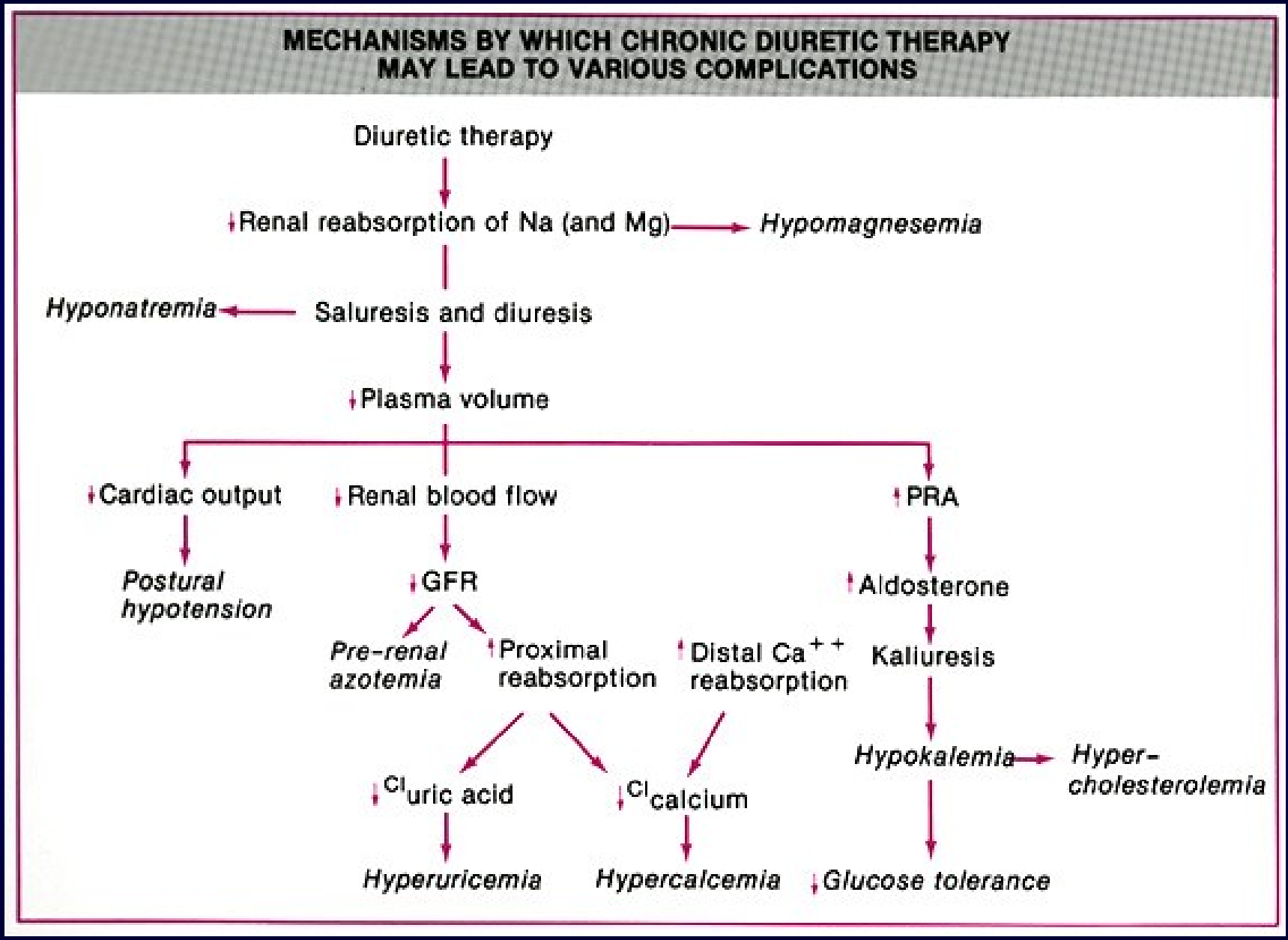
Manual of Medicine

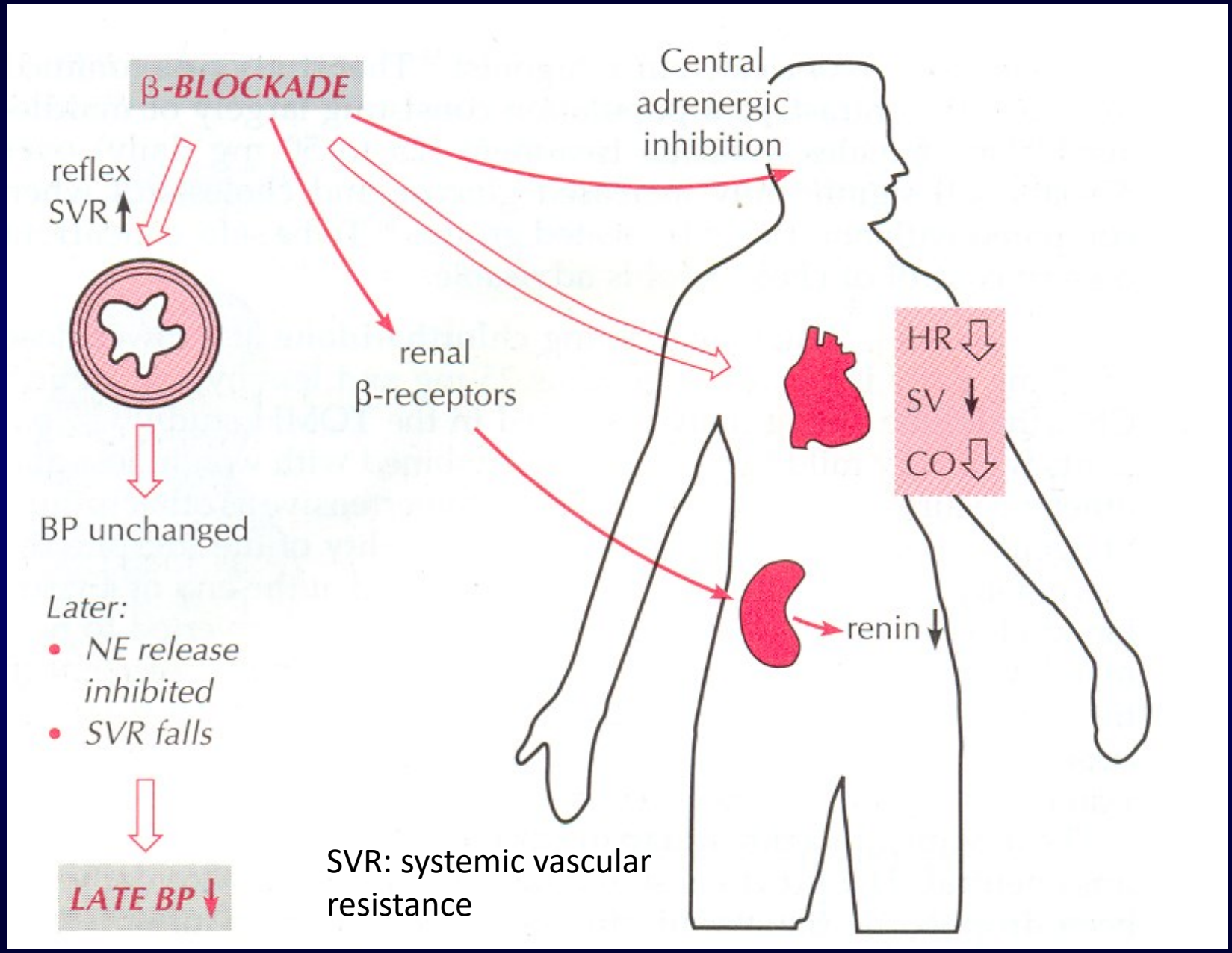

Glomerulus
Proximal Convoluted Tubule
Loop of Henle
Distal Convoluted Tubule
Collecting Duct
Reabsorption & Secretion
Solution concentration
Reabsorption & Secretion
Afferent arteriole
NSAIDs
PGI2 & PGE2
Vasodilators
Carbonic Anhydrase Inhibitors
Thiazides
H2O
NaHCO3
Glucose
Loop diuretics
NaCl
ENaC (Aldosterone)
Aldosterone antagonists
Efferent arteriole
Ang II
Vasoconstrictor
ACE-Is
Osmotic diuretics
Na/K/2Cl
Na
K
Cortex
Outer Medulla
Descending Limb
Ascending Limb
Vasopressin
H2O (ADH)
ADH antagonists


Proximal convoluted tubule
SGLT2i
SGLT2
Na+ Glucose
Distal convoluted tubule
Potassium sparing diuretics
K+ Na+
Glomerulus
ENaC
Thiazides
Na+Cl-
Na-Cl cotransporter
NaHCO3
Carbonic anhydrase inhibitors
Na+/K+
2Cl-
Collecting duct
Na-K-2Cl cotransporter
Loop of Henle
Loop diuretics
Vaptans
H2O
Aquaporin

SGLT-2 Inhibitors




MECHANISMS BY WHICH CHRONIC DIURETIC THERAPY MAY LEAD TO VARIOUS COMPLICATIONS
Diuretic therapy
↓Renal reabsorption of Na (and Mg)
Hypomagnesemia
Hyponatremia
Saluresis and diuresis
↓Plasma volume
↓Cardiac output
↓Renal blood flow
↑PRA
Postural hypotension
↓GFR
↑Aldosterone
Pre-renal azotemia
↑Proximal reabsorption
↑Distal Ca++ reabsorption
Kaliuresis
Hypokalemia
Hyper-cholesterolemia
↓Cl uric acid
↓Cl calcium
Hyperuricemia
Hypercalcemia
↓Glucose tolerance

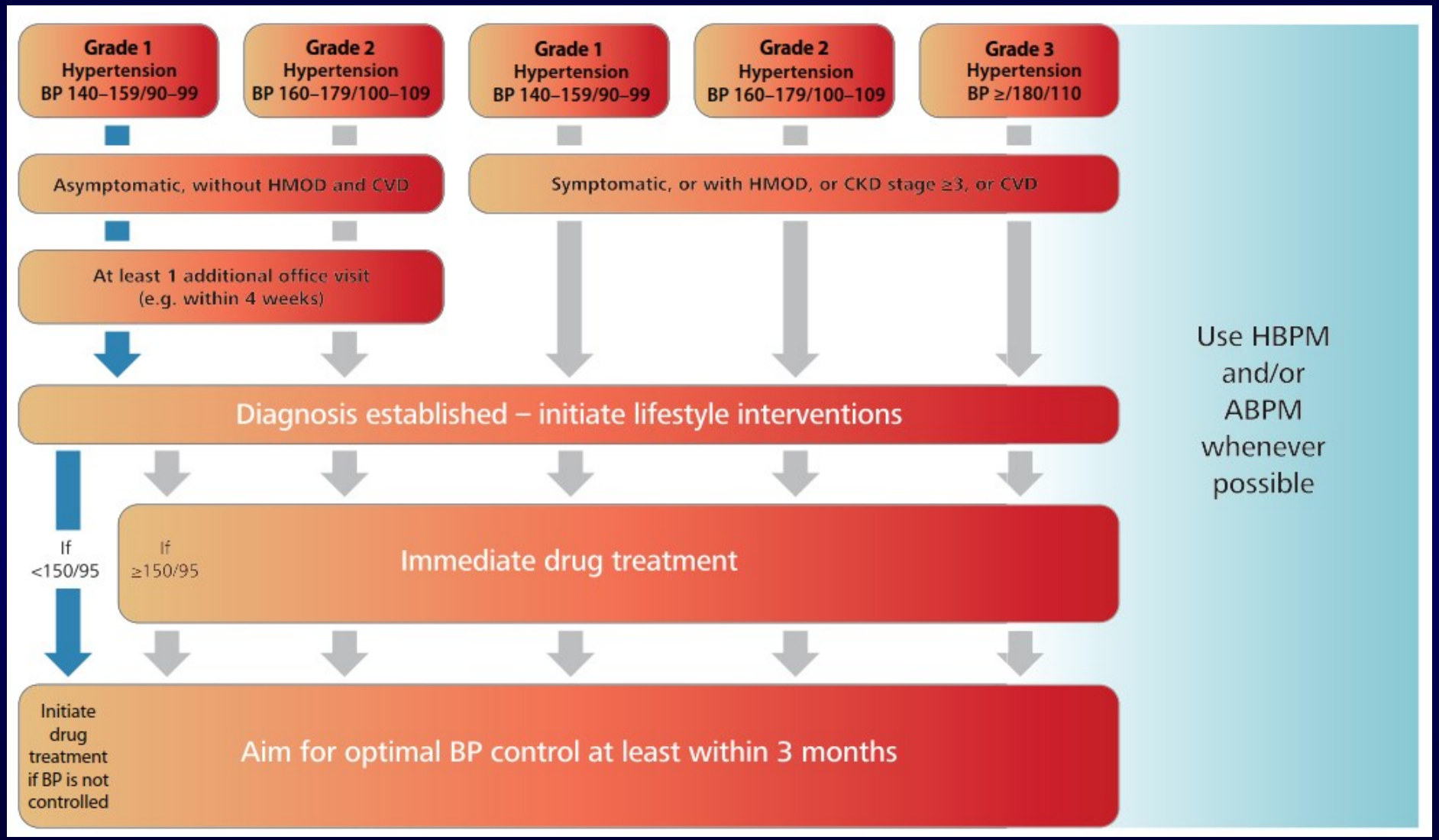


SVR: systemic vascular resistance

Φάρμακα ΑΥ: Αντενδείξεις & Προφυλάξεις

Drug class	Contraindications	Cautious use
ACEi	• Pregnancy • Women planning pregnancy • Previous angioneurotic edema • Severe hyperkalemia (e.g. potassium >5.5 mmol/l) • Bilateral renal artery stenosis or stenosis in solitary (functional) kidney	• Women of child-bearing potential without reliable contraception
ARB	• Pregnancy • Women planning pregnancy • Severe hyperkalemia (e.g. potassium >5.5 mmol/l) • Bilateral renal artery stenosis or stenosis in solitary (functional) kidney	• Women of child-bearing potential without reliable contraception
Beta-blocker	• Severe asthma • Any high-grade sino-atrial or atrioventricular block • Bradycardia (e.g. heart rate <60 bpm)	• Asthma • Glucose intolerance • Athletes and physically active patients
DHP-CCB		• Tachyarrhythmia • Heart failure (HFrEF, class III or IV) • Preexisting severe leg edema
Non-DHP-CCB (verapamil, diltiazem)	• Any high-grade sino-atrial or AV block • Severe LV dysfunction (LVEF <40%), HFrEF • Bradycardia (e.g. heart rate <60 bpm) • Co-medications susceptible to significant drug interactions mediated by P-gp or CYP3A4	• Constipation
Thiazide/Thiazide-like diuretics	• Hyponatremia • CKD due to obstructive uropathy • Sulfonamide allergies	• Gout • Glucose intolerance • Pregnancy • Hypercalcemia • Hypokalemia • Cancer patients with bone metastasis
MRA	• Severe hyperkalemia (e.g. potassium >5.5 mmol/l) • eGFR <30 ml/min/1.73 m^2	• Co-medications susceptible to significant drug interactions mediated by P-gp or CYP3A4 for eplerenone

Διάγνωση & Αρχική Διαχείριση ΑΥ



ESH Guidelines 2023

Lifestyle τροποποίηση : Δίαιτα

- Φρούτα
- Λαχανικά
- Χαμηλά λίπη
- DASH diet

Dietary Sodium

Restrict to target range of 65-100 mmol/day

(Most of the salt in food is hidden and comes from processed food)

Dietary Potassium

If required, daily dietary intake >80 mmol

~~**Calcium supplementation**~~

No conclusive studies for hypertension

~~**Magnesium supplementation**~~

No conclusive studies for hypertension

http://www.hc-sc.gc.ca/hpfb-dgpsa/onpp-bppn/food_guide_rainbow_e.html

DASH diet:
Dietary Approaches to Stop Hypertension

Lifestyle τροποποίηση : Φυσική δραστηριότητα

Απαραίτητη για μείωση ΑΠ

F	Frequency	- 3-4 μέρες την εβδομάδα
I	Intensity	- Μέτρια
T	Time	- 30-45 min
T	Type	Δυναμική - Περπάτημα, jogging - Ποδήλατο - Κολύμπι

For patients who are prescribed pharmacological therapy: Exercise should be prescribed as adjunctive therapy

Lifestyle τροποποίηση : Αλκοόλ

Χαμηλή κατανάλωση

- 0-2 ποτά/ημέρα
- Άνδρες: max 14 / εβδομάδα
- Γυναίκες: max 8 / εβδομάδα

1 ποτό = 1 μπύρα,1 ποτήρι κρασί, 1 ποτήρι 40% αλκοόλ

Lifestyle τροποποίηση : Stress

Θεραπεία

Τροποποποίηση συμπεριφοράς

Τεχνικές χαλάρωσης

Lifestyle τροποποίηση : Απώλεια βάρους

BMI > 25 επί HTN

- Ενθάρυνση
- Στόχος BMI: 18.5-24.9 kg/m^2

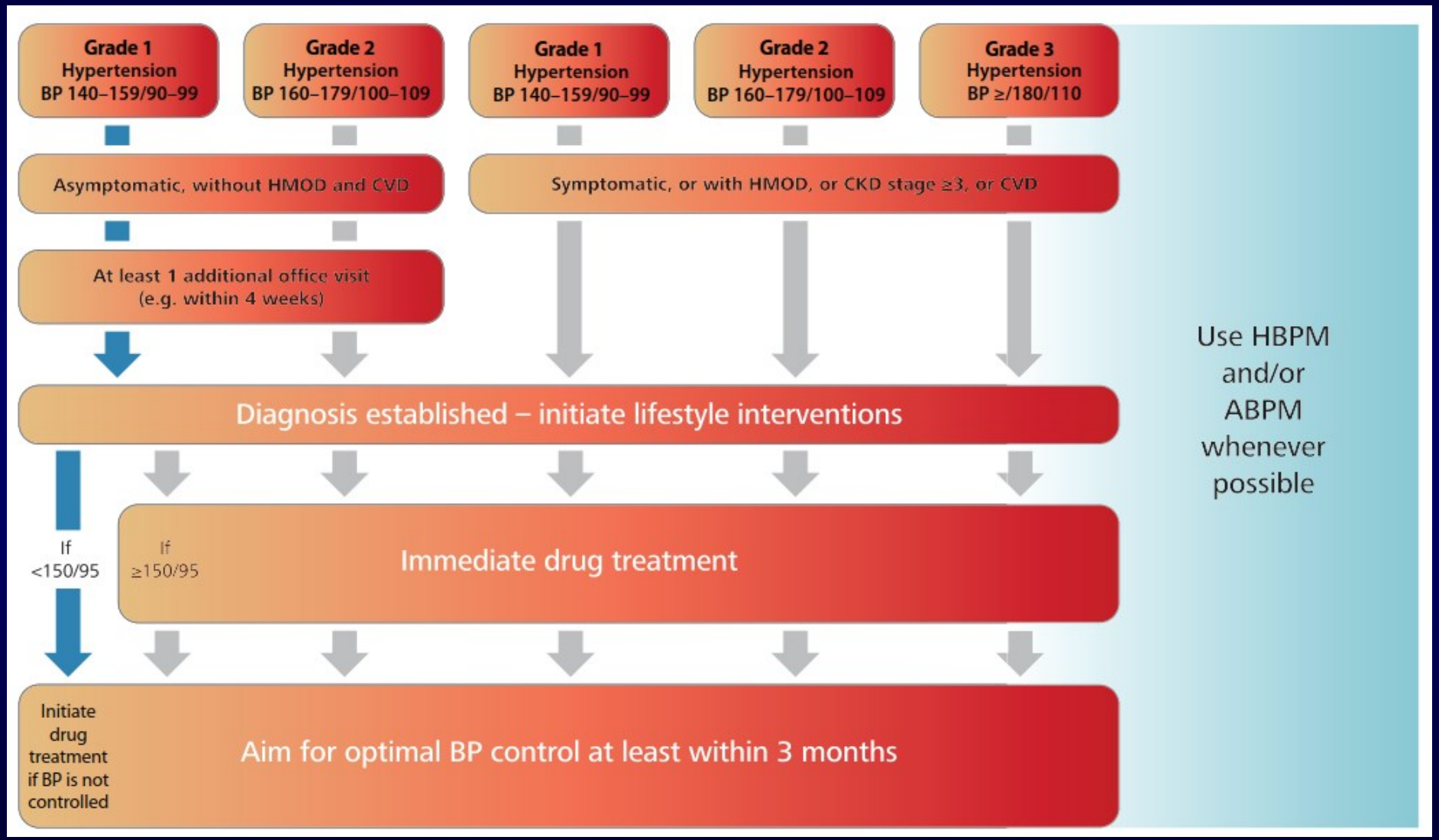
Εκπαίδευση, άσκηση, συμπεριφορά

Lifestyle τροποποίηση : Αποτελέσματα

Παρέμβαση	Μεταβολή	SBP/DBP
Αλάτι	100 mmol/day	-5.8 / -2.5
Απώλεια βάρους	- 4.5 kg	-7.2 / -5.9
Αλκοόλ	- 2.7 ποτά/ημέρα	-4.6 / -2.3
Άσκηση	3 φορές/εβδομάδα	-10.3 / -7.5
Δίαιτα	DASH diet	-11.4 / -5.5

DASH diet:
Dietary Approaches
to Stop Hypertension

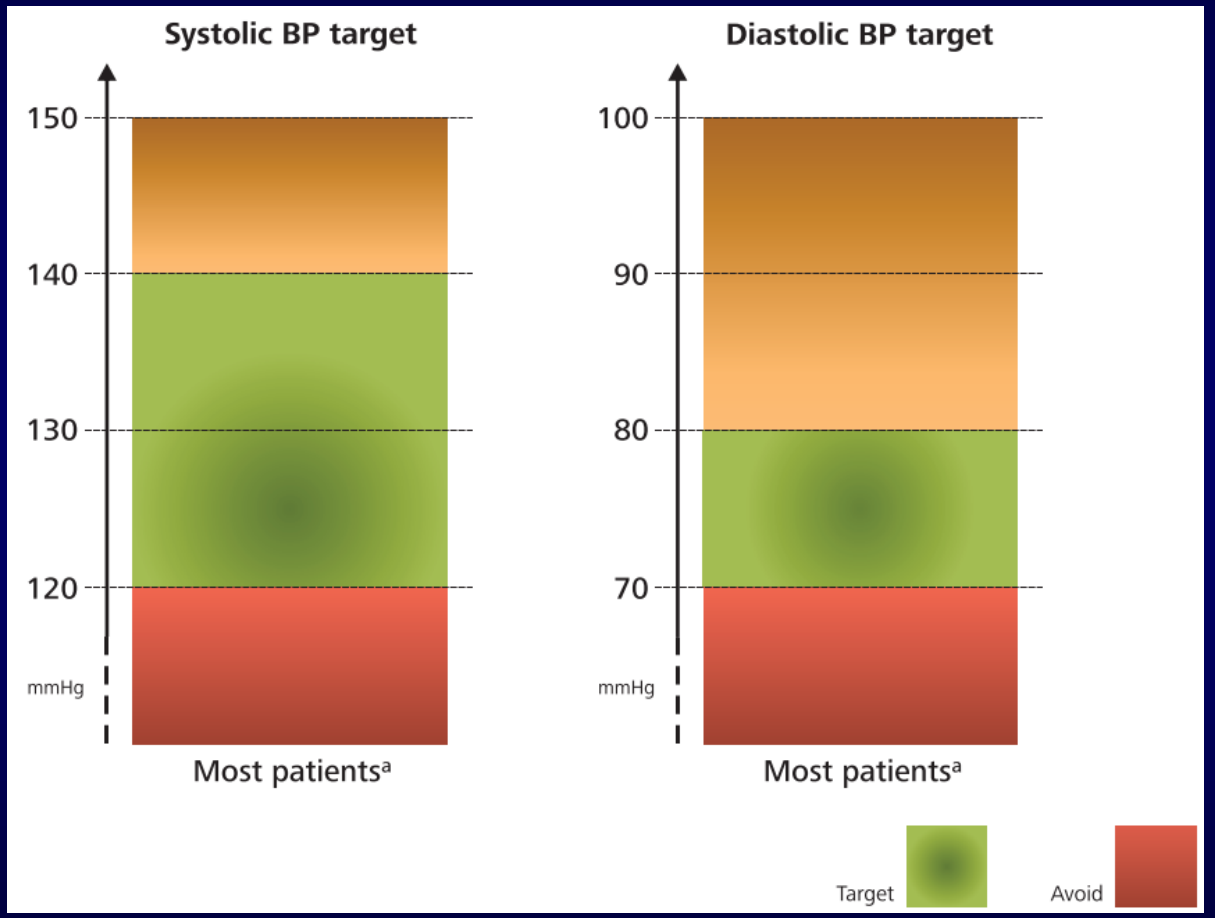
Διάγνωση & Αρχική Διαχείριση ΑΥ



ESH Guidelines 2023

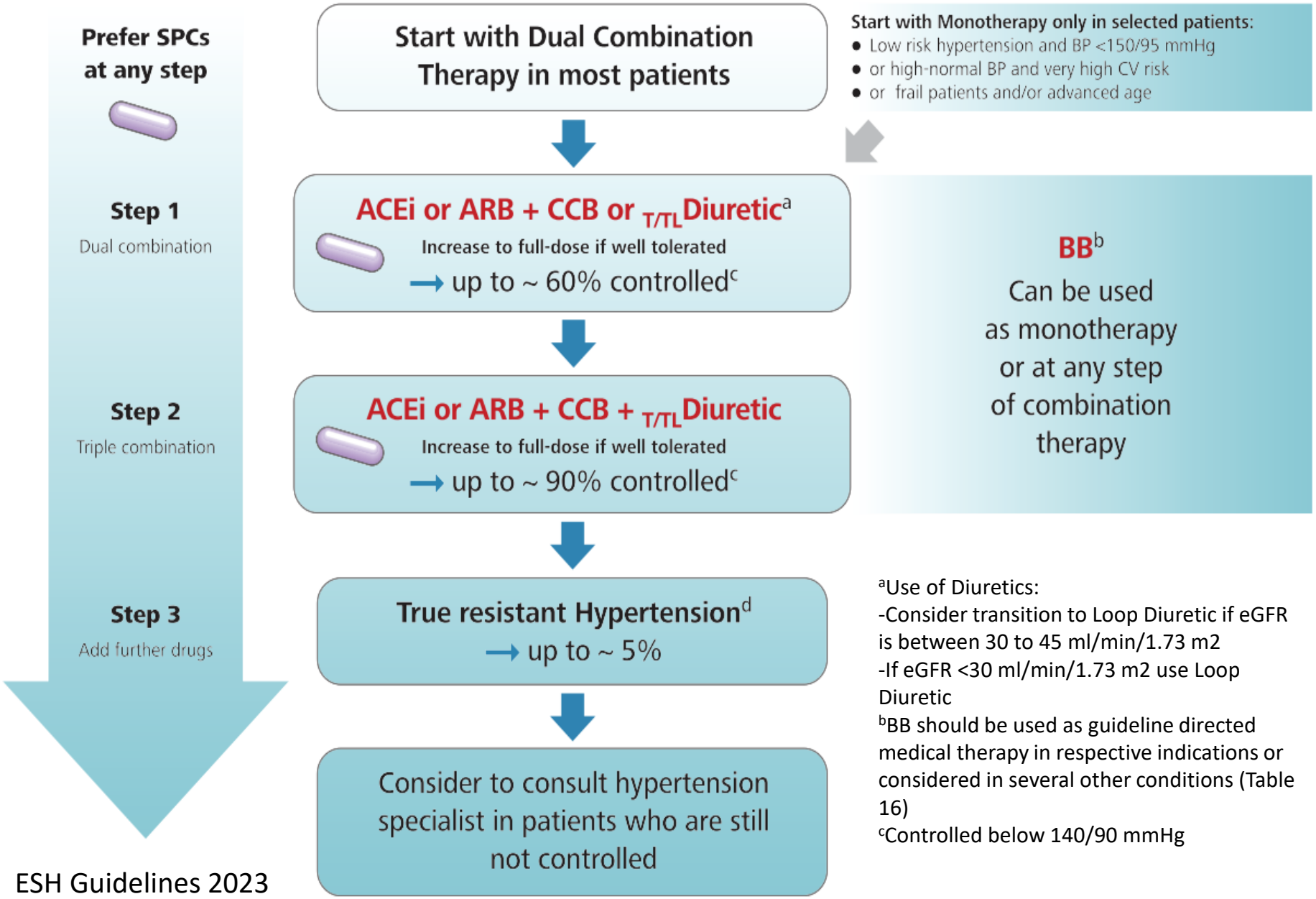
Στόχοι Θεραπείας

Office BP targets in the general adult hypertensive population.
[a]The first objective of antihypertensive treatment should be to lower BP to <140/80 mmHg in most patients, because this accounts for the major portion of the protective effect of BP-lowering.
[a]If drug treatment is well tolerated, treated SBP values should be targeted to 130 mmHg or lower in most patients up to 79 years old.
[a]Despite the smaller incremental benefit, an effort should be made to reach a BP range of 120–129/70–79 mmHg in patients up to 79 years old, but only if treatment is well tolerated. Evidence on the advantages of this lower BP target range is not available or unequivocal in a number of clinically important subgroups of patients (e.g. patients with LVH, CKD, or ISH). These issues are discussed in the sections on special conditions (see Sections 17 to 20).
[a]In patients at least 80 years old who are not frail, the first objective of antihypertensive treatment is to lower BP below 150 mmHg. However, a SBP target range between 130-139 mmHg may be considered, if well tolerated.
[a]In very frail patients, treatment targets should be individualized.



ESH Guidelines 2023

Γενική Στρατηγική Αντιμετώπιση ΑΥ



[a]Use of Diuretics:
-Consider transition to Loop Diuretic if eGFR is between 30 to 45 ml/min/1.73 m2
-If eGFR <30 ml/min/1.73 m2 use Loop Diuretic

[b]BB should be used as guideline directed medical therapy in respective indications or considered in several other conditions (Table 16)

[c]Controlled below 140/90 mmHg

ESH Guidelines 2023

Αποτυχία δυο φαρμάκων

Τριπλή ή τετραπλή αγωγή

Ελέχγω

Ανυπακοή?
Δευτερογενής ΗΤΝ;
Φάρμακα/συνήθειες;
Λευκή μπλούζα;
Ανθεκτική ΗΤΝ;

Ανθεκτική Υπέρταση

Όταν δεν επιτυγχάνεται ο στόχος (ΑΠ γραφείου <140/90 mmHg) μετά από αλλαγές lifestyle και βέλτιστη αγωγή με 3 ή περισσότερα φάρμακα (Thiazide/Thiazide-like diuretic, RAS blocker και CCB)

ΑΙΤΙΑ

- Εσφαλμένη μέτρηση
- Αλάτι
- Ανεπαρκή διουρητικά
- Φάρμακα
  - Ανεπαρκείς δόσεις
  - Αλληλεπιδράσεις (πχ., nonsteroidal anti-inflammatory drugs (NSAIDs), illicit drugs, sympathomimetics, oral contraceptives)
  - Over-the-counter (OTC) drugs & herbal supplements
- Αλκοόλ
- Δευτερογενής HTN

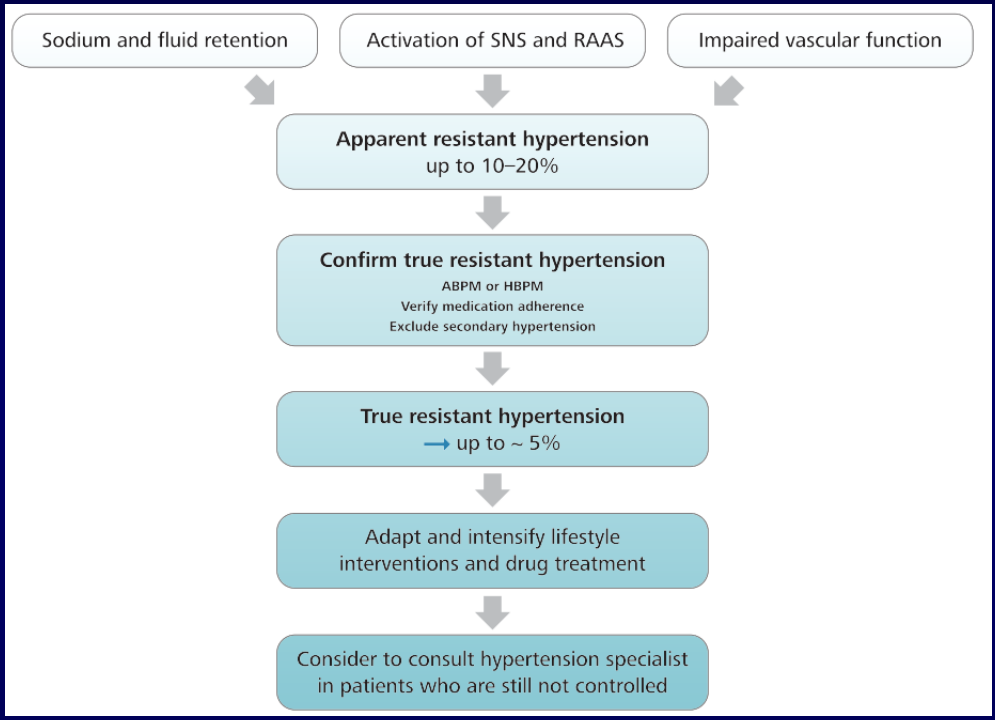
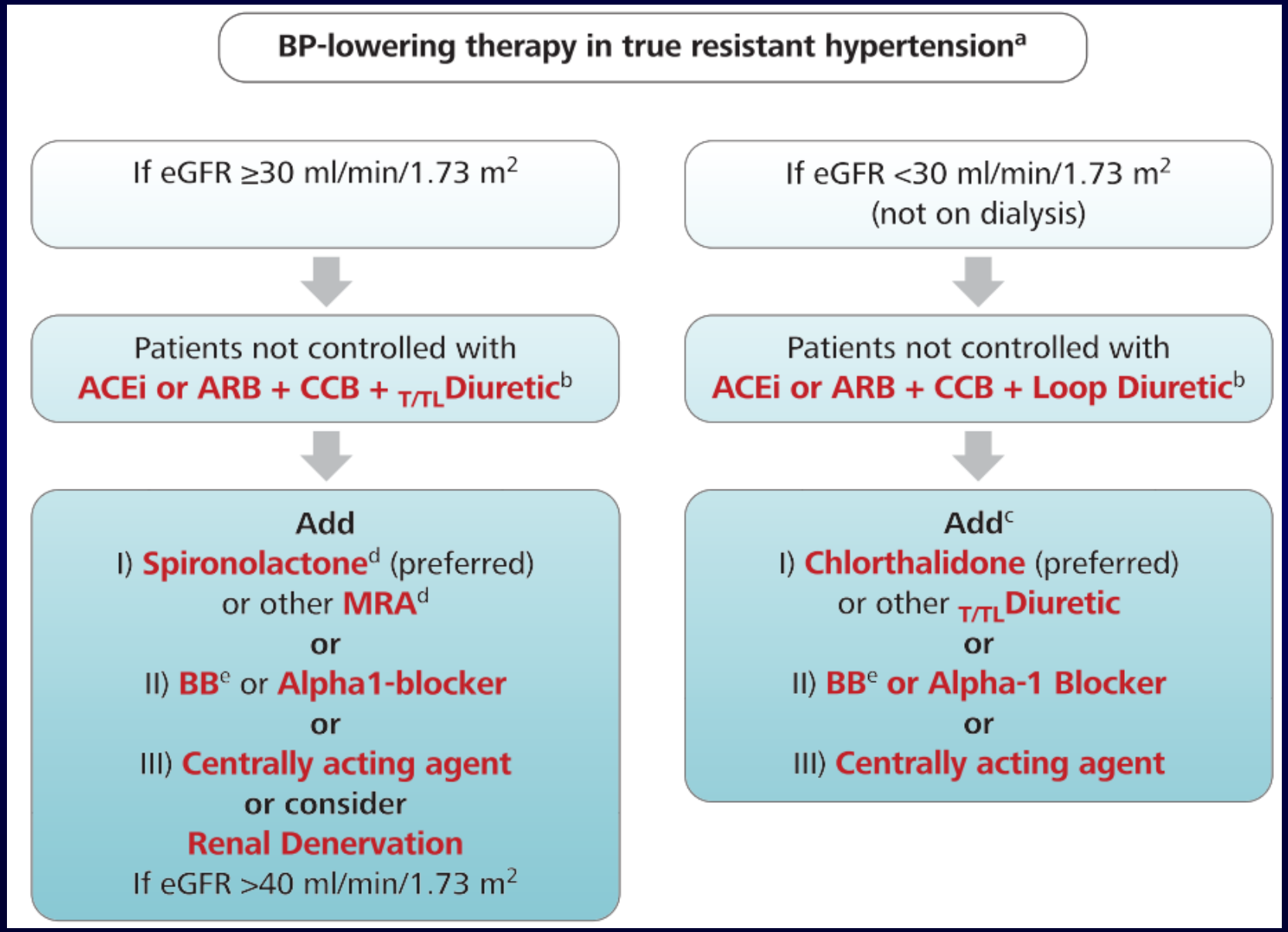


TABLE 7. Drug/substance exacerbators and inducers of hypertension

Drug/substance [32–43]	Comments on specific drugs and substances[a]
Nonsteroidal Antiinflammatory Drugs (NSAIDs)	No difference or an increase of up to 3/1 mmHg with celecoxib 3/1 mmHg increase with nonselective NSAIDs No increase in blood pressure with aspirin NSAIDs can antagonize the effects of RAAS inhibitors and beta blockers
Combined oral Contraceptive pill	6/3 mmHg increase with high doses of estrogen (>50 μg of estrogen and 1–4 μg progestin)
Antidepressants	2/1 mmHg increase with SNRI (selective norepinephrine and serotonin reuptake inhibitors) Increased odds ratio of 3.19 of hypertension with tricyclic antidepressant use No increases in blood pressure with SSRI (selective serotonin reuptake inhibitors)
Acetaminophen	Increased relative risk of 1.34 of hypertension with almost daily acetaminophen use
Other medications	Steroids Antiretroviral therapy: inconsistent study findings for increased blood pressure Sympathomimetics: pseudoephedrine, cocaine, amphetamines Antimigraine serotonergics Recombinant human erythropoeitin Calcineurin inhibitors Antiangiogenesis and kinase inhibitors 11β-hydroxysteroid dehydrogenase type 2 inhibitors
Herbal and other Substances [44,45]	Alcohol, Ma-huang, Ginseng at high doses, Liquorice, St. John's Wort, Yohimbine

[a]Average increase in blood pressure or risk of hypertension. However, the effect of these medications/substances on blood pressure may highly vary between individuals.

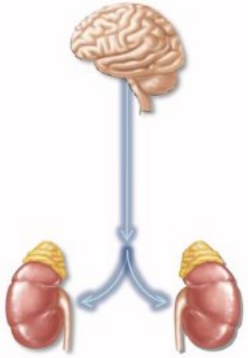
Αντιμετώπιση Ανθεκτικής Υπέρτασης



Renal Nerves

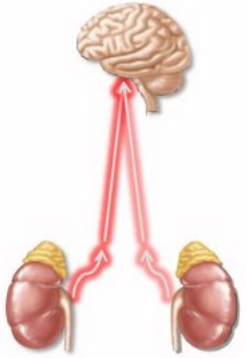
Renal Nerves and the SNS

Efferent Sympathetics



- Renin release → RAAS
- Na absorption
- Renal blood flow (TPR)

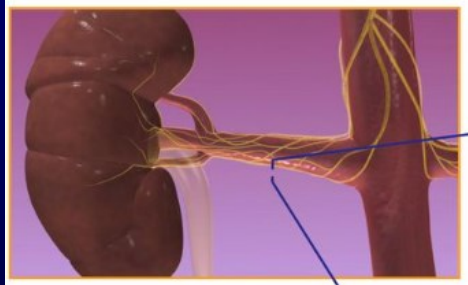
Afferent Renal Sympathetics



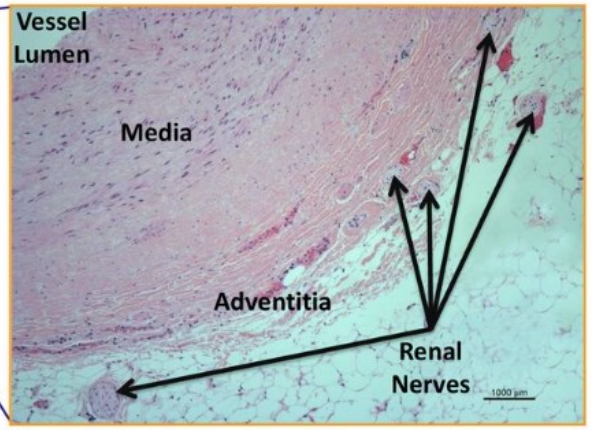
The kidney is a source of central sympathetic activity, sending signals to the CNS

Adapted from Schlaich MP, et al. *Hypertension*. 2009;54:1195-1201.

Renal Nerve Anatomy



- Nerves arise from T10-L2
- The nerves arborize around the artery and primarily lie within the adventitia



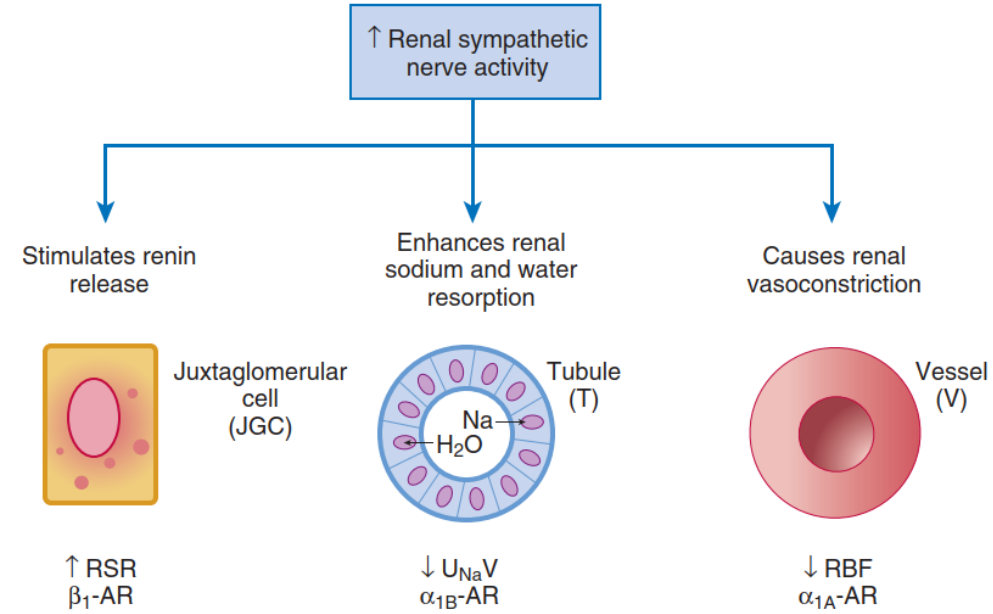


FIGURE 43-6 Effects of increased renal sympathetic nerve activity on the three renal neuroeffectors: the juxtaglomerular granular cells with increased renin secretion rate (RSR) via stimulation of the beta-1 adrenoceptors (β_1-AR); the renal tubular epithelial cells (T) with increased renal tubular sodium reabsorption and decreased urinary sodium excretion (UNaV) via stimulation of alpha-1β adrenoceptors –(α_{1B}-AR); and the renal vasculature (V) with decreased renal blood flow (RBF) via stimulation of α_{1A}-AR. *(From DiBona GF: Physiology in perspective: The wisdom of the body. Neural control of the kidney. Am J Physiol Regul Integr Comp Physiol 289:R633, 2005.)*

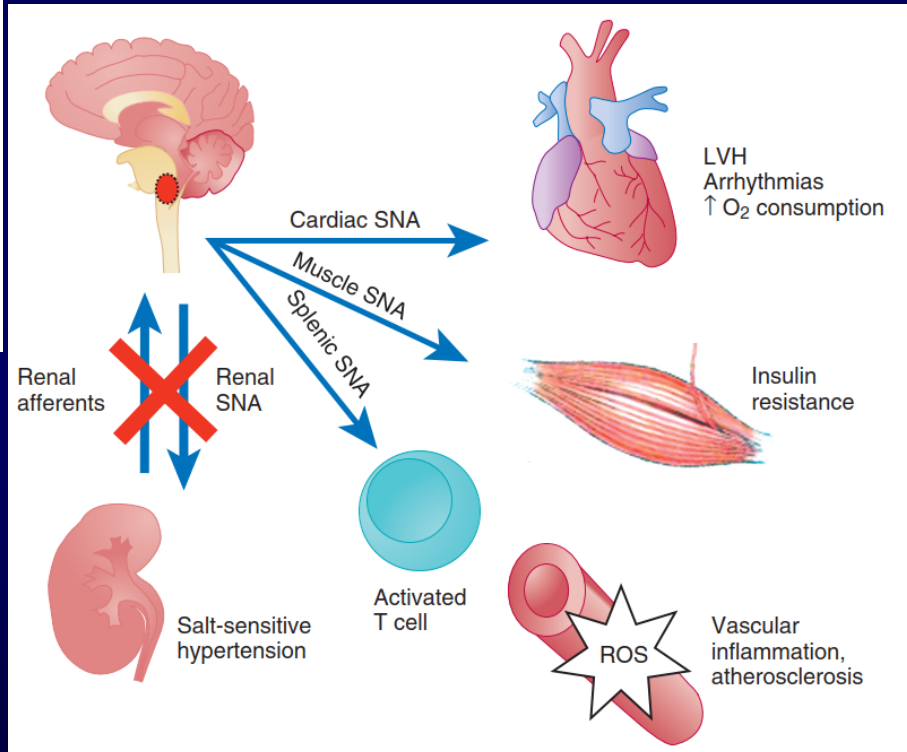
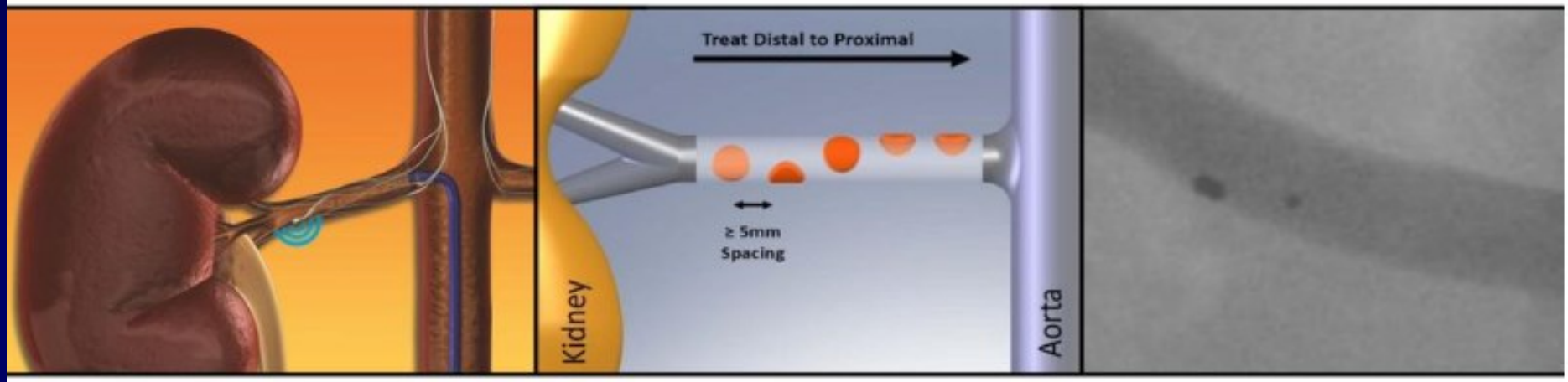


FIGURE 43-7 Conceptual framework by which denervation of renal afferents explains ancillary benefits of catheter-based renal denervation. In patients with drug-resistant hypertension, overactivity of efferent renal sympathetic nerve activity (SNA) contributes to salt-sensitive hypertension, whereas overactivity of renal sensory (afferent) nerves triggers sustained reflex increases in cardiac SNA (leading to left ventricular hypertrophy, arrhythmias, and increased oxygen consumption), in skeletal muscle SNA (leading to insulin resistance), and in splenic SNA (activating T cells, which are honed to vascular smooth muscle, stimulating reactive oxygen species [ROS] that promote vascular inflammation and atherosclerosis).

Novel Catheter-Based Approach to Denervation



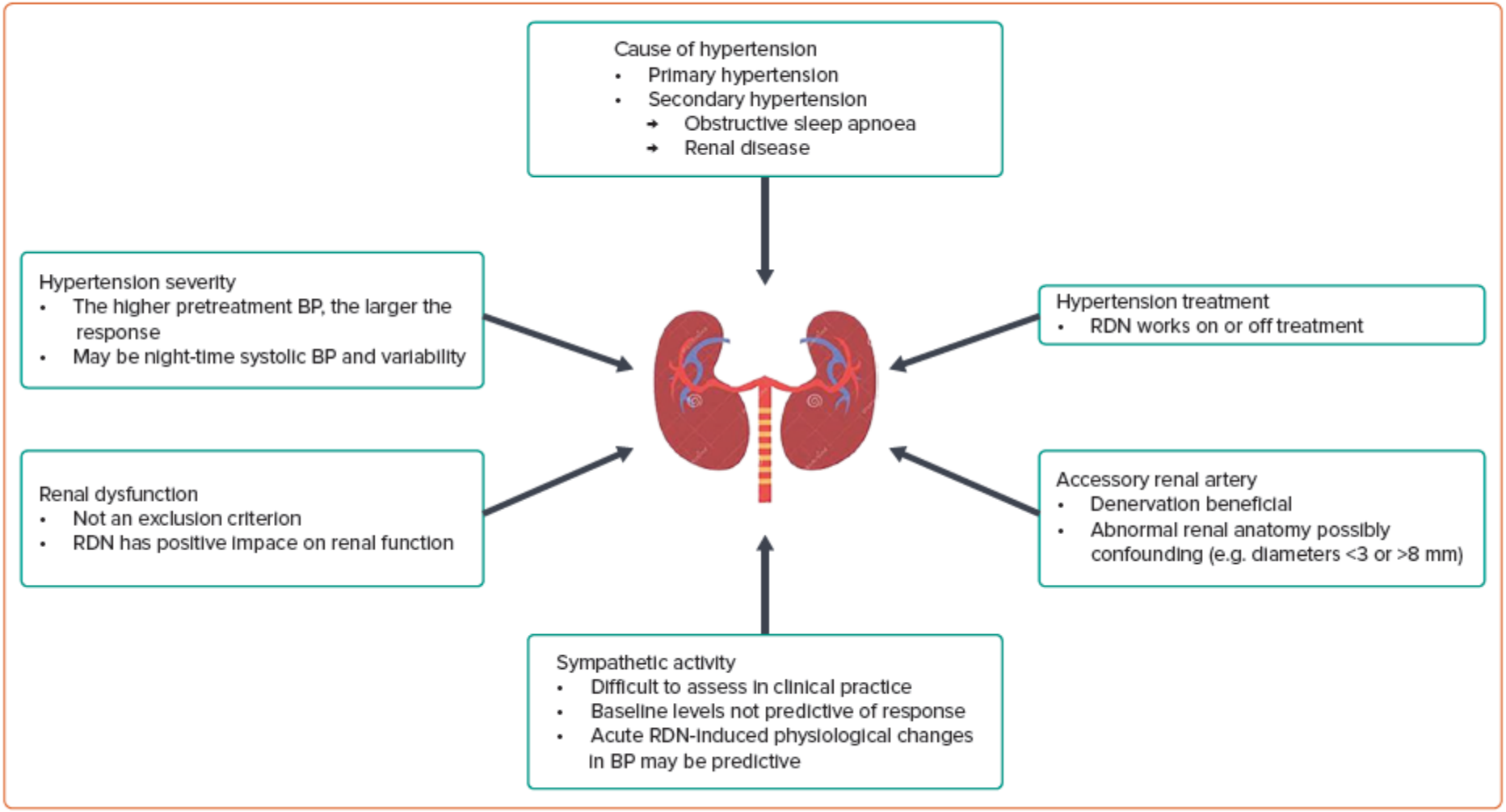
- Standard interventional technique
- 4-6 two-minute treatments per artery
- Proprietary RF generator
  - Automated
  - Low power, 8W maximum
  - Built-in safety algorithms

Table 1: Summary of Sham-controlled Renal Denervation Trials and Real-world Evidence to Date

	SPYRAL HTN-OFF MED[2]	SPYRAL HTN-ON MED[3,4]	RADIANCE-HTN SOLO[1]	RADIANCE HTN-TRIO[5]	RADIANCE II (PIVOTAL)[18]	Global SYMPLICITY Registry[6]
Design	Randomised sham-controlled trial	Randomised sham-controlled trial	Multicentre international single-blind randomised sham-controlled trial	Multicentre international single-blind randomised sham-controlled trial	Randomised sham-controlled trial	Prospective open-label single-arm multicentre all-comer observational study
No. sites/ patients	44 sites	25 sites	21 sites	28 sites	224 patients	>3,000 patients
Aim	To assess the efficacy of RDN in patients not taking antihypertensive medications	To assess the efficacy of RDN in patients continuing to take antihypertensive medications	To assess the effect of ultrasound RDN on BP reduction in patients with mild-to-moderate HTN controlled on 1–2 antihypertensive medications or uncontrolled on 0–2 medications	To assess the effect of ultrasound RDN on BP reduction in a drug-resistant population on ≥3 antihypertensive medications	To demonstrate the effectiveness and safety of the Paradise System in subjects with stage 2 hypertension on 0–2 medications	To evaluate the impact of medication burden on the BP-lowering effect of RDN
Primary endpoint	Baseline-adjusted change in 24-h SBP	Change in BP from baseline to 6 months in the RDN versus sham control group	Mean change in daytime ambulatory SBP from baseline to 2 months in the RDN versus sham control group	Mean change in daytime ambulatory SBP from baseline to 2 months in the RDN versus sham control group	1. Incidence of MAE from baseline to 30 days after the procedure 2. Change in mean daytime ambulatory SBP from baseline to 2 months after the procedure.	N/A
Results	Primary endpoint was met with posterior probability of superiority >0.999	1. At 6 months, the primary efficacy endpoint was met: mean baseline-adjusted treatment difference in 24-h SBP was –7.0 mmHg (95% CI [–12.0, –2.1]; p=0·0059) and in 24-h DBP was –4.3 mmHg (95% CI [–7.8, –0.8]; p=0.0174) 2. At 36 months, treatment differences for mean ambulatory were: −5.9 mmHg (95% CI [−10.1, −1.8]; p=0.0055) for DBP; −11.0 mmHg (95% CI [−19.8, −2.1]; p=0·016) for morning SBP; and −11.8 mmHg (95% CI [−19.0, −4.7]; p=0.0017) for night-time SBP	Primary endpoint was met: there was a greater reduction in daytime ambulatory SBP at 2 months in the RDN than sham control group (mean [±SD] –8.5 ± 9.3 versus –2.2 ± 10.0 mmHg, respectively)	Primary endpoint was met: there was a greater reduction in daytime ambulatory SBP at 2 months with the RDN than sham procedure (median [IQR] –8.0 [–16.4, 0.0] versus –3.0 [–10.3, 1.8] mmHg, respectively; median between-group difference –4.5 mmHg, 95% CI [–8.5, –0.3], baseline-adjusted p=0.022)	Primary endpoint was met: 1. The Paradise system had a mean change in daytime ambulatory SBP of –7.9 mmHg, compared with –1.8 mmHg in the sham arm (significant between-group difference of –6.3 mmHg; p<0.0001) 2. No MAEs from baseline to 30 days	RDN resulted in significant and clinically meaningful reductions in both office and 24-h BP that were sustained out to 3 years after the procedure
Key findings	RDN was superior to a sham procedure to safely lower BP in the absence of antihypertensive medications	A significant decrease in 24-h ambulatory BP from baseline to 6 months was achieved in the RDN group and was sustained within the TTR over the long-term follow-up of 3 years Further, RDN decreased BP independent of the baseline antihypertensive medication burden and without increasing the medication burden over time	Ultrasound RDN of main renal arteries and accessory arteries >4 mm in diameter achieved a similar significant drop in daytime ambulatory SBP at 2 months in patient populations with: HTN with no medications; and with HTN resistant to a standardised triple combination of medications`		Results consistent with the prior SOLO (off-medication) and TRIO (on triple antihypertensive treatment) trials	The reduction in BP achieved after RDN treatment was independent of baseline antihypertensive medications and did not result in increased medication burden over time The benefit of RDN on BP through to 3 years was consistent within patients with and without CKD A subgroup analysis of the Global SYMPLICITY Register showed similar office SBP reductions at 3 years in patients with OSA, diabetes or current smokers[41]

BP = blood pressure; CKD = chronic kidney disease; DBP = diastolic blood pressure; MAE = major adverse events; OSA = obstructive sleep apnoea; RDN = renal denervation; SBP = systolic blood pressure TTR = target treatment range.

Figure 1: Considerations in Patient Selection to Predict a Better Response to Renal Denervation



BP = blood pressure; RDN = renal denervation. Adapted from: Li and Phillips 2022.[29] Used with permission from Dove Medical Press.

Υπερτασικές Κρίσεις

- Σοβαρή ΗΤΝ ΜΕ συνοδό οξεία βλάβη οργάνων στόχων (π.χ. Εγκεφαλοπάθεια, έμφραγμα, ΟΠΟ, εκλαμψία, ΑΕΕ, αιμορραγία, διαχωρισμός αορτής) => εισαγωγή και IV θεραπεία.

- Σοβαρή ΗΤΝ ΧΩΡΙΣ συνοδό οξεία βλάβη οργάνων στόχων => άμεση έναρξη αγωγής Ρ.Ο.

Τύποι Κλινικών Περιστατικών

- Ασθενείς με Κακοήθη Υπέρταση (σοβαρή υπέρταση συνήθως grade 3) σχετιζόμενη με ευρήματα στην βυθοσκόπηση, οξεία καρδιακή ανεπάρκεια, και οξεία επιδείνωση νεφρικής λειτουργίας → κακή πρόγνωση
- Ασθενείς με σοβαρή υπέρταση σχετιζόμενη με άλλες κλινικές παθήσεις που χρήζουν επείγουσας μείωσης της ΑΠ, πχ οξύς αορτικός διαχωρισμός, οξεία μυοκαρδιακή ισχαιμία ή οξεία καρδιακή ανεπάρκεια
- Ασθενείς με απότομη σοβαρή υπέρταση λόγω φαιοχρωμοκυτώματος σχετιζόμενη με βλάβη οργάνου
- Έγκυες γυναίκες με σοβαρή υπέρταση ή προ-εκλαμψία

Διαγνωστικός Έλεγχος σε Ασθενείς με Υπερτασική Κρίση

Common tests for all potential causes
Fundoscopy is a critical part of the diagnostic workup
12-lead ECG
Haemoglobin, platelet count, fibrinogen
Creatinine, eGFR, electrolytes, LDH, haptoglobin
Urine albumin:creatinine ratio, urine microscopy for red cells, leucocytes, casts
Pregnancy test in women of child-bearing age
Specific tests by indication
Troponin, CK-MB (in suspected cardiac involvement, e.g. acute chest pain or acute heart failure) and NT-proBNP
Chest X-ray (fluid overload)
Echocardiography (aortic dissection, heart failure, or ischaemia)
CT angiography of thorax and/or abdomen in suspected acute aortic disease (e.g. aortic dissection)
CT or MRI brain (nervous system involvement)
Renal ultrasound (renal impairment or suspected renal artery stenosis)
Urine drug screen (suspected methamphetamine or cocaine use)

CK-MB = creatinine kinase-muscle/brain; CT = computed tomography; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; LDH = lactate dehydrogenase; MRI = magnetic resonance imaging; NT-proBNP = N-terminal pro-B natriuretic peptide.

TABLE 12. Hypertensive Emergencies Requiring Immediate blood pressure lowering

Clinical presentation	Timeline and target BP	First line treatment	Alternative
Malignant hypertension with or without TMA or acute renal failure	Several hours, MAP –20% to –25%	Labetalol Nicardipine	Nitroprusside Urapidil
Hypertensive encephalopathy	Immediate, MAP –20% to –25%	Labetalol Nicardipine	Nitroprusside
Acute ischaemic stroke and BP >220 mmHg systolic or >120 mmHg diastolic	1 h, MAP –15%	Labetalol Nicardipine	Nitroprusside
Acute ischaemic stroke with indication for thrombolytic therapy and BP >185 mmHg systolic or >110 mmHg diastolic	1 h, MAP –15%	Labetalol Nicardipine	Nitroprusside
Acute hemorrhagic stroke and systolic BP >180 mmHg	Immediate, systolic 130 < BP < 180 mmHg	Labetalol Nicardipine	Urapidil
Acute coronary event	Immediate, SBP <140 mmHg	Nitroglycerine Labetalol	Urapidil
Acute cardiogenic pulmonary edema	Immediate, SBP <140 mmHg	Nitroprusside or Nitroglycerine (with loop diuretic)	Urapidil (with loop diuretic)
Acute aortic disease	Immediate, SBP <120 mmHg and heart rate <60 bpm	Esmolol and Nitroprusside or Nitroglycerine or nicardipine	Labetalol or Metoprolol
Eclampsia and severe pre-eclampsia/HELLP	Immediate, SBP <160 mmHg and DBP <105 mmHg	Labetalol or nicardipine and magnesium sulphate	

BP = blood pressure; bpm = beats per min; DBP = diastolic blood pressure; HELLP = haemolysis, elevated liver enzymes, and low platelets; i.v. = intravenous; MAP = mean arterial pressure; SBP = systolic blood pressure