

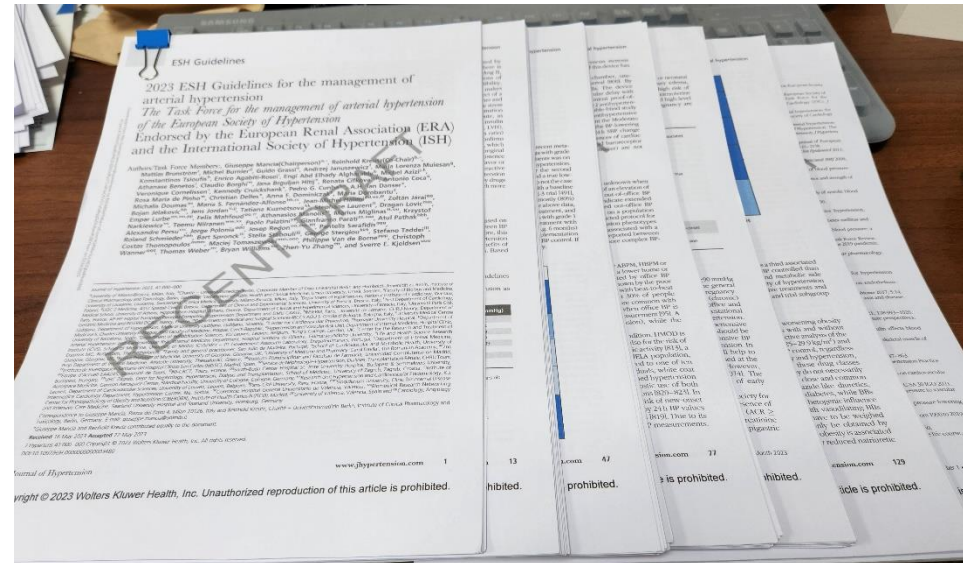
Cutting edge treatment of Hypertension

이해영

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What is new and has changed in 2023 ESH guideline?

- ❖ Modified and simplified criteria for evidence grading recommendations
- ❖ Thorough description of office, ambulatory and home BP measurements
- ❖ New HMOD measurements in hypertension work-up
- ❖ New CV risk factors and update on CV risk assessment
- ❖ Secondary forms of hypertension
- ❖ Lifestyle interventions
- ❖ Threshold and targets for drug Tx
- ❖ True-resistant hypertension
- ❖ Treatment in Elderly, CKD, Af, DM,
- ❖ Follow-up of hypertension



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Isolated systolic hypertension of the young (ISHY)

- ❖ ISH is present not only in older persons but also in young and very young individuals, more commonly in male individuals.
 - ✓ ISHY may be present also in children and adolescents
 - ✓ often associated with overweight and obesity
 - ✓ more common in athletes than sedentary people
- ❖ Increased cardiac output, heart rate and stroke volume are the predominant hemodynamic abnormalities
 - ✓ Higher peripheral pulse pressure
 - ✓ Central BP measurement help to identify ISHY patients at lower risk

Recommendations and statements	CoR	LoE
Due to the frequent presence of a pronounced white-coat effect, out-of-office BP measurement is recommended.	I	C
Central BP measurement can be considered to identify ISHY individuals at low CV risk to detect spurious hypertension, if available.	II	C
Close follow-up and lifestyle interventions are recommended.	I	C
In individuals with high out-of-office BP or high central BP, particularly with other CV risk factors or HMOD, BP lowering drug treatment can be considered.	II	C

Isolated diastolic hypertension

- ❖ Prevalence: 2.5 -7.8%
 - ✓ Peak between 30 and 39 years
 - ✓ Decrease in the fifth and sixth decades (<15%)
 - ✓ Almost no case above 70 years of age
- ❖ Generally younger, of male sex, consume more alcohol and tobacco, and are more frequently diabetic patients (Metabolic syndrome)

Recommendations and statements	CoR	LoE
Periodic BP evaluation and lifestyle interventions are recommended for all patients with IDH.	I	C
Despite the absence of dedicated RCTs in IDH, it is recommended that the BP lowering drug treatment should follow the general treatment strategy.	II	C

Night-time hypertension and BP phenotypes

- ❖ Isolated nocturnal hypertension has been found to be present in 9.2–12.9% of adults
- ❖ More prevalent in men with high-normal BP and a high CV risk profile, African Americans, older, obese and diabetic patients, patients with CKD and individuals with WCH.
- ❖ A steady increase in asleep BP and a decline in the nocturnal BP fall occur with aging

Recommendations and statements	CoR	LoE
It is recommended to assess night-time BP using ABPM because it is more predictive for outcomes than daytime BP, and because nocturnal hypertension, non-dipping and reverse dipping are associated with increased CV risk	I	B
For the identification of night-time BP phenotypes, repeating ABPM is necessary, because of poor reproducibility.	I	B
Elevated night-time BP may be reduced by antihypertensive treatment.	II	C
In the general hypertensive population morning dosing or bedtime dosing results in similar outcome.	I	B

가정 혈압 측정을 적극적으로 이용할 수 있음

- 5009 HT patients in 500 primary care clinics in Korea
- 7 days of SBPM, daily duplicated in the morning and evening
- Acceptable SBPM values, recorded > 10 / 14 times of scheduled measurement, acquired in 4435 patients (> 89%)
- Mean SD of HBPM of 4.6 ± 2.8 / 3.6 ± 1.9 mmHg

722 Principle: 외래 방문 7일전, 아침/저녁 1일 2회, 한번 측정 시 2회 반복
고혈압 진단시, 약제 변경 2주 뒤, 매 3개월마다

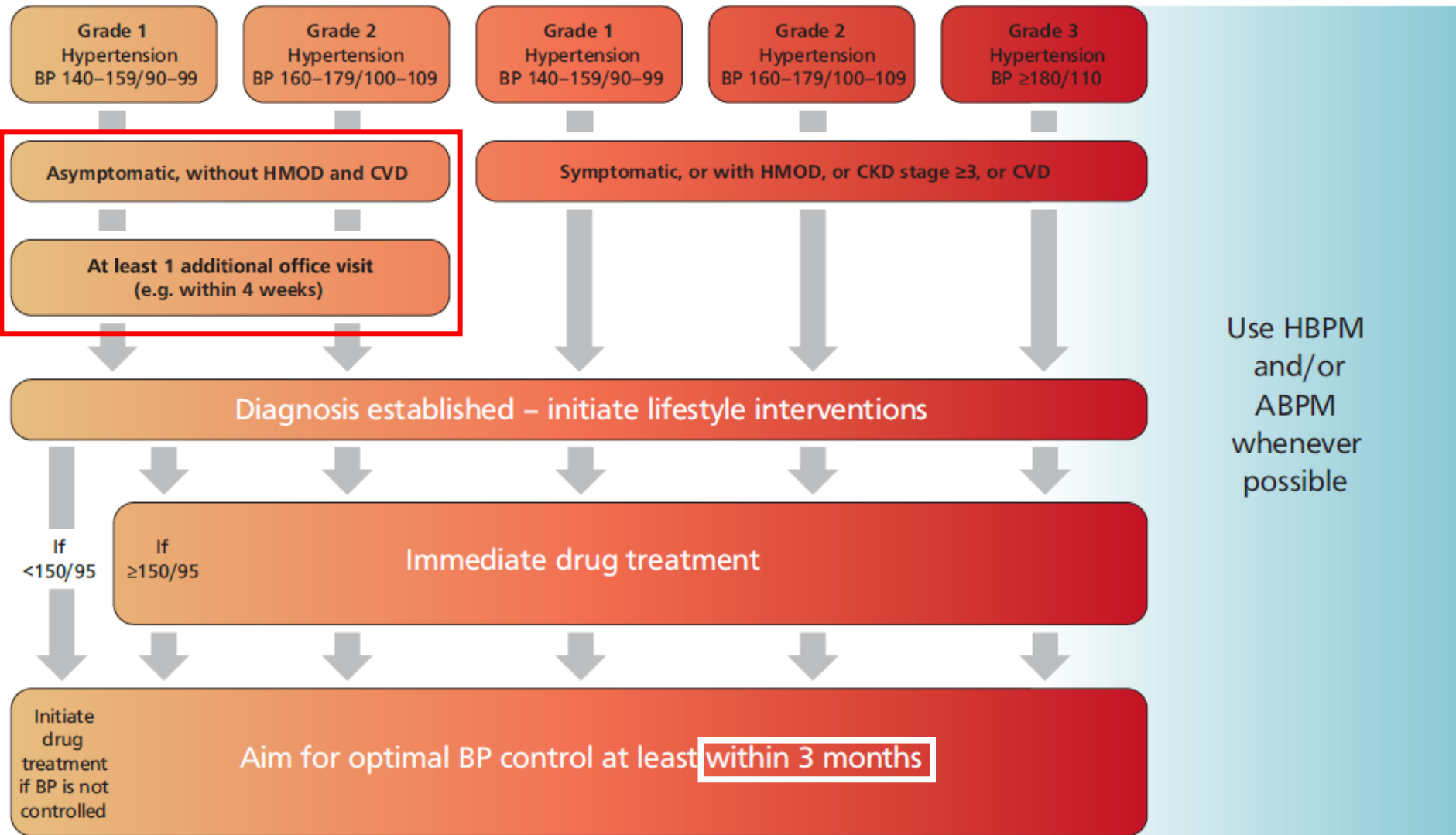
- ✓ Prevalence and risk factors of masked hypertension identified by multiple self blood pressure measurement Hae-Young Lee, Jeong Bae Park, on behalf of KEY2 investigators. Hypertension, 2008
- ✓ 722 Principle proposed by Taiwan Hypertension Society

가정 혈압과 진료실 혈압 (2022년 대한고혈압학회 진료지침)

	진료실혈압	24시간 활동혈압 일일평균혈압	24시간활동 혈압 주간평균혈압	가정혈압
수축기혈압	140	130	135	135
수축기혈압	130	125	130	130

- ❖ 진료실 혈압 140/90에 상응하는 가정 혈압은 135/85mmHg.
- ❖ 가정혈압의 간격은 진료실 혈압보다 좁아 가정 혈압의 145mmHg은 진료실 혈압 160mmHg에 상응한다는 보고가 있음.

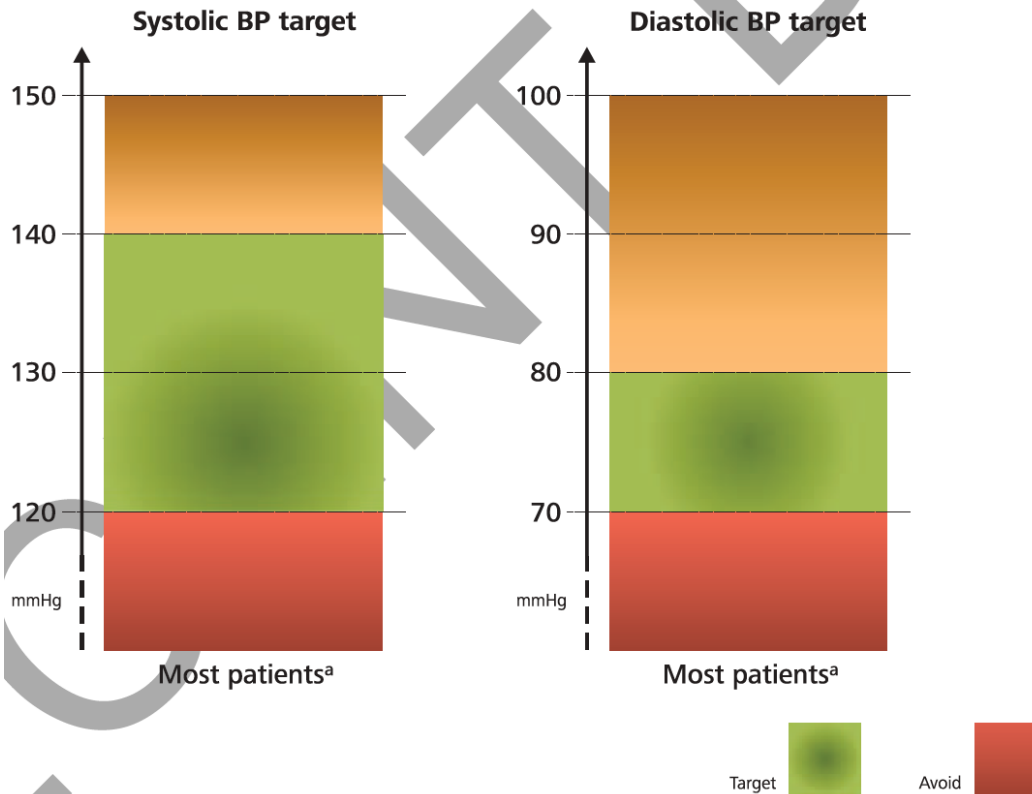
Diagnosis by office BP and initial management of HT



Diagnosis by office BP and initial management of HT

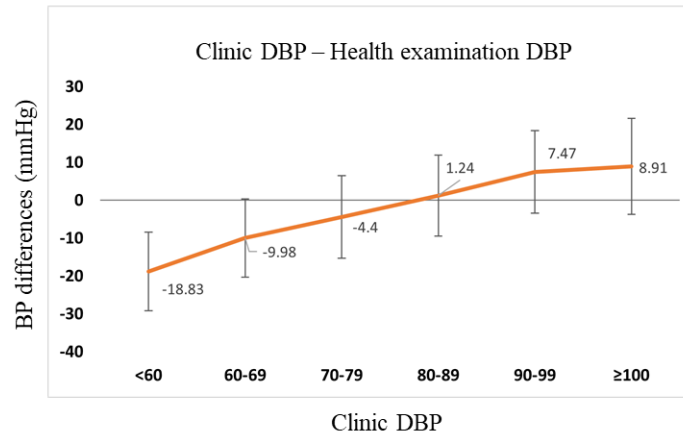
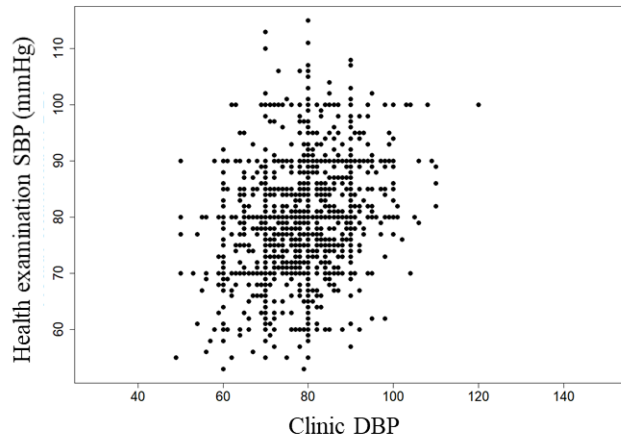
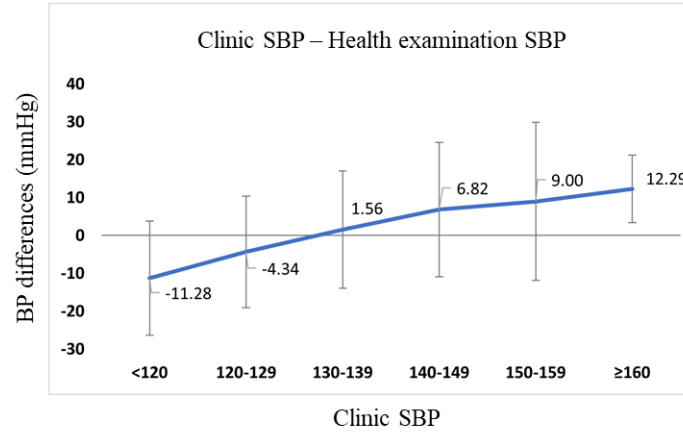
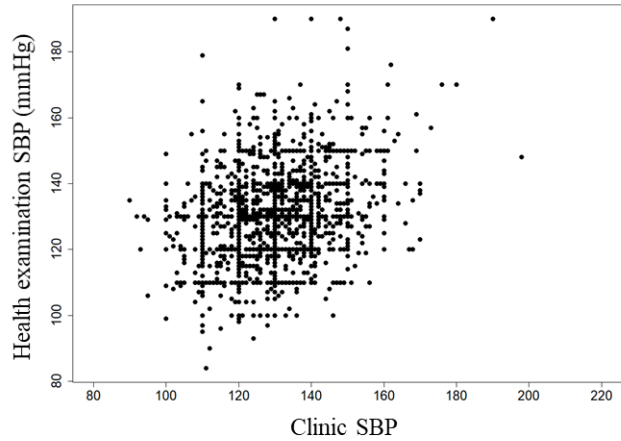
Recommendations and statements	CoR	LoE
In patients 18 to 79 years, the recommended office threshold for initiation of drug treatment is 140 mmHg for SBP and/or 90 mmHg for DBP.	I	A
In patients ≥ 80 years, the recommended office SBP threshold for initiation of drug treatment is 160 mmHg.	I	B
However, in patients ≥ 80 years a lower SBP threshold in the range 140 – 160 mmHg may be considered.	II	C
The office SBP and DBP thresholds for initiation of drug treatment in frail patients should be individualized.	I	C
In adult patients with a history of CVD, predominantly CAD, drug treatment should be initiated in the high-normal BP range (SBP ≥ 130 or DBP ≥ 80 mmHg).	I	A

Office BP targets in general adult HT population



- ❖ First <140/80 mmHg in most patients
- ❖ If drug treatment is well tolerated, SBP \leq 130 mmHg
- ❖ **BP range of 120–129/70–79 mmHg in patients up to 79 years old**
- ❖ In patients \geq 80 yo not frail, first < 150/80 mmHg, then SBP 130-139 mmHg
- ❖ In very frail patients, treatment targets should be individualized.

BP differences between (Usual) clinic and (Standard) health examination



The importance of (needless to say but often overlooked) accurate BP measurement should be emphasized more.

IT'S THE Precise BP measurement



STUPID!!

Lee HY, et al. Korean Hypertension Cohort, Paper submitted

고립성 수축기 고혈압의 70%는 이완기 혈압이 낮지 않음



AMISH

Aprovel for **M**anagement of **I**solated **S**ystolic **H**ypertension

- Primary: To evaluate non-inferiority of irbesartan (and/or hydrochlorothiazide fixed combination) to amlodipine (and/or hydrochlorothiazide) in reducing the office seated SBP in elderly patients with ISH
- 전세계적인 4상 연구였으나 70% 이상의 screening failure를 보여 결국 380명만을 등록하고 조기 종료

고혈압 약제 치료 총론

Five major drug classes including, ACEis, ARBs, BBs, CCBs, and Thiazide/Thiazide-like diuretics have effectively reduced BP and CV events in RCTs. These drugs and their combinations are recommended as the basis of antihypertensive treatment strategies.

I

A

Initiation of therapy with a two-drug combination is recommended for most hypertensive patients. Preferred combinations should comprise a RAS blocker (either an ACE inhibitor or an ARB) with a CCB or Thiazide/Thiazide-like diuretic. Other combinations of the five major drug classes can be used.

I

A

Initiation with monotherapy can be considered in patients with:

- grade 1 hypertension and low-risk if BP is only marginally elevated (less than 150 mmHg SBP and 95 mmHg DBP)
- high-normal BP and very high CV risk,
- frailty and/or and advance age.

I

C

If BP is not controlled with the initial two-drug combination by using the maximum recommended and tolerated dose of the respective components, treatment should be increased to a three-drug combination, usually a RAS blocker + CCB + Thiazide/Thiazide-like diuretic.

I

A

고혈압 약제 치료 총론

- Start with Monotherapy only in selected patients:
- Low risk hypertension and BP <150/95 mmHg
 - or high-normal BP and very high CV risk
 - or frail patients and/or advanced age

Prefer SPCs
at any step



Step 1
Dual combination

Start with Dual Combination
Therapy in most patients

ACEi or ARB + CCB or T/TL Diuretic^a
Increase to full-dose if well tolerated
→ up to ~ 60% controlled^c



Step 2
Triple combination

ACEi or ARB + CCB + T/TL Diuretic
Increase to full-dose if well tolerated
→ up to ~ 90% controlled^c



Step 3
Add further drugs

True resistant Hypertension^d
→ up to ~ 5%

Consider to consult hypertension
specialist in patients who are still
not controlled

BB^b
Can be used
as monotherapy
or at any step
of combination
therapy

고혈압 약제 특기 기술: Thiazide/Thiazide like

- ❖ In meta-analyses of RCTs, Thiazide/Thiazide-like appear to be more effective than other major drug classes in preventing HF
 - ✓ This finding may be influenced by the results of the ALLHAT study, in which patients largely under a background diuretic treatment were rolled over to comparison drugs, with a possible emergence of HF symptoms previously under diuretic-based symptomatic control.
- ❖ The thiazide-like diuretics, chlorthalidone and indapamide, are more potent and have a longer duration of action compared with hydrochlorothiazide, but a greater incidence of side effects has been reported for chlorthalidone in some studies.
 - ✓ A meta-analysis of placebo-controlled studies based on thiazides, chlorthalidone, and indapamide found similar effects for the three types of diuretics on CV outcomes.
- ❖ No major difference between hydrochlorothiazide and chlorthalidone has been observed in a large observational cohort study [LEGEND] and open-label study, DCP.
 - ✓ In DCP, patients who were already on hydrochlorothiazide were randomized to either chlorthalidone or hydrochlorothiazide continuation.
 - ✓ Patients on treatment with hydrochlorothiazide 25 or 50mg were converted to 12.5 or 25mg chlorthalidone
 - ✓ No difference in CV outcomes between the two drugs was found, except for patients with a prior stroke in whom there was a greater benefit with chlorthalidone.
- ❖ Potassium plays an important role in the metabolic effects of Thiazide/Thiazide like.
- ❖ A recent placebo-controlled study has demonstrated that chlorthalidone effectively lowers BP and albuminuria in patients with uncontrolled HT and CKD stage 4 (eGFR <30 ml/min/1.73m²) when added to the therapy of these conditions, which often includes a loop diuretic (60% of the patients)

고혈압 약제 특기 기술: Beta blockers

❖ BBs should be used at initiation of Tx GDMT, examples:

- ✓ Heart failure with reduced ejection fraction HFrEF
- ✓ Anti-ischemic therapy in chronic coronary syndromes
- ✓ Heart rate control in atrial fibrillation

Selected indications with guideline directed medical therapy for BBs

Chronic coronary syndromes, antiischemic therapy

Postmyocardial infarction: arrhythmias, angina, known incomplete re-vascularization, HF

Acute coronary syndrome

HFrEF and HFpEF if coronary disease (ischemia), arrhythmias and tachycardia

Atrial fibrillation: prevention, rhythm control, heart rate control

Women with child-bearing potential/planning pregnancy

Hypertension disorders in pregnancy

Selected other conditions in which therapy with BBs can be favourable

Hypertension with elevated resting heart rate >80 bpm

Emergency, urgency and parenteral administration

Perioperative hypertension

Major noncardiac surgery

Excessive pressor response to exercise and stress

Hyperkinetic heart syndrome

Postural orthostatic tachycardia syndrome

Orthostatic hypertension

OSA

Peripheral arterial disease with claudication

COPD

Portal hypertension, cirrhosis-related esophageal varices and recurrent variceal bleeding

Glaucoma

Thyrotoxicosis, hyperthyroidism

Hyperparathyroidism in uremia

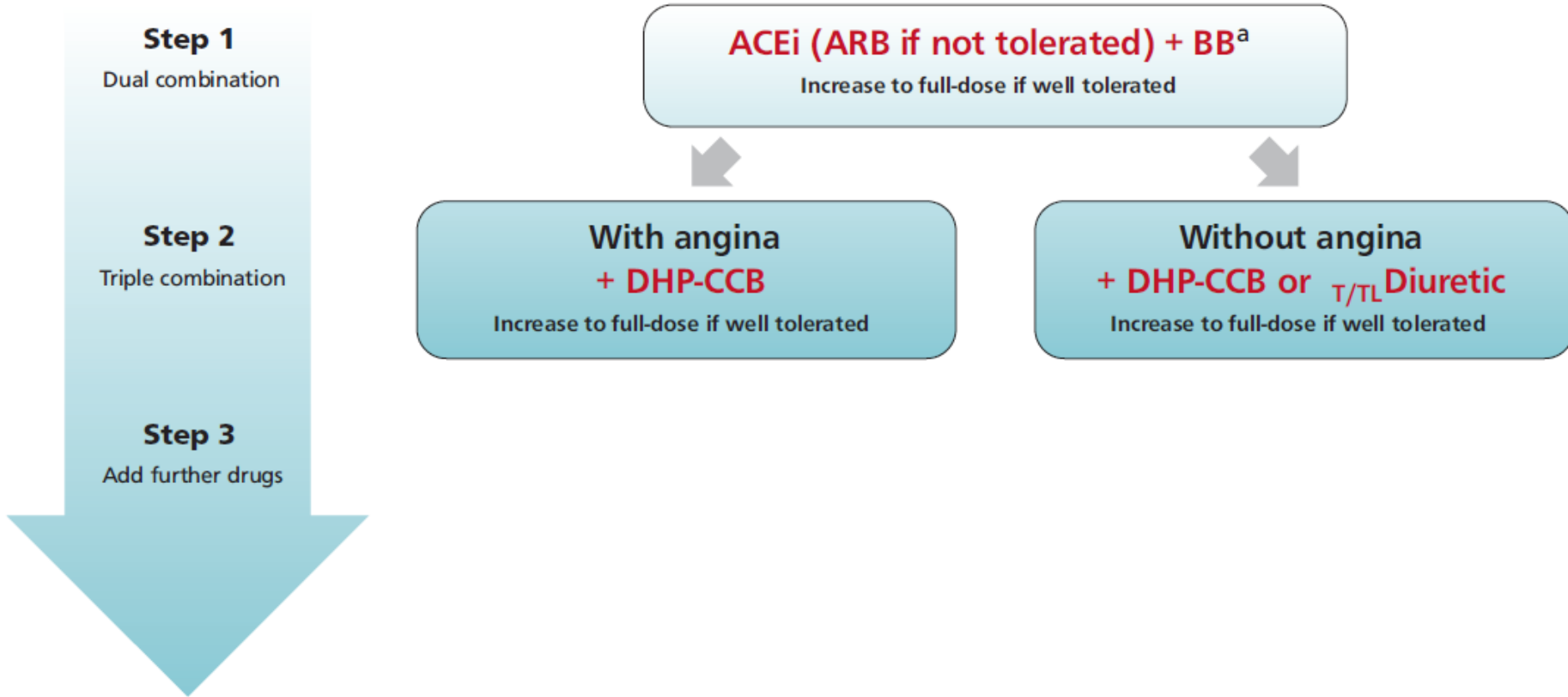
Migraine headache

Essential tremor

Performance anxiety and anxiety disorders

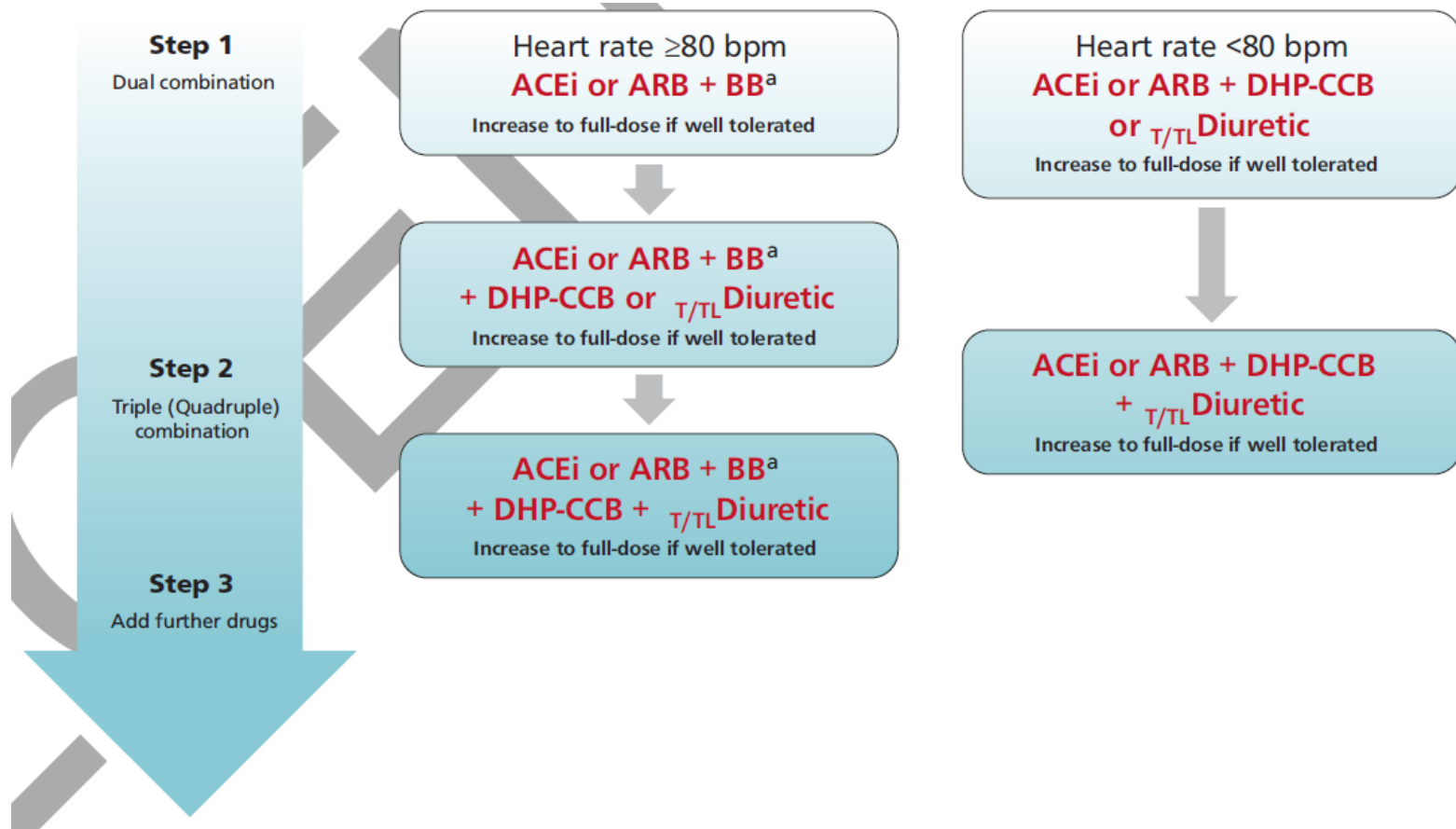
Psychiatric disorders (posttraumatic stress)

관상동맥질환자에서의 고혈압 조절



- ❖ Target HR < 80 BPM (60-80) with BB, if contraindicated with non-DHP CCB
- ❖ Drug treatment should be initiated in the high-normal BP range (SBP ≥130 or DBP ≥80 mmHg).

심방세동환자에서의 고혈압 조절

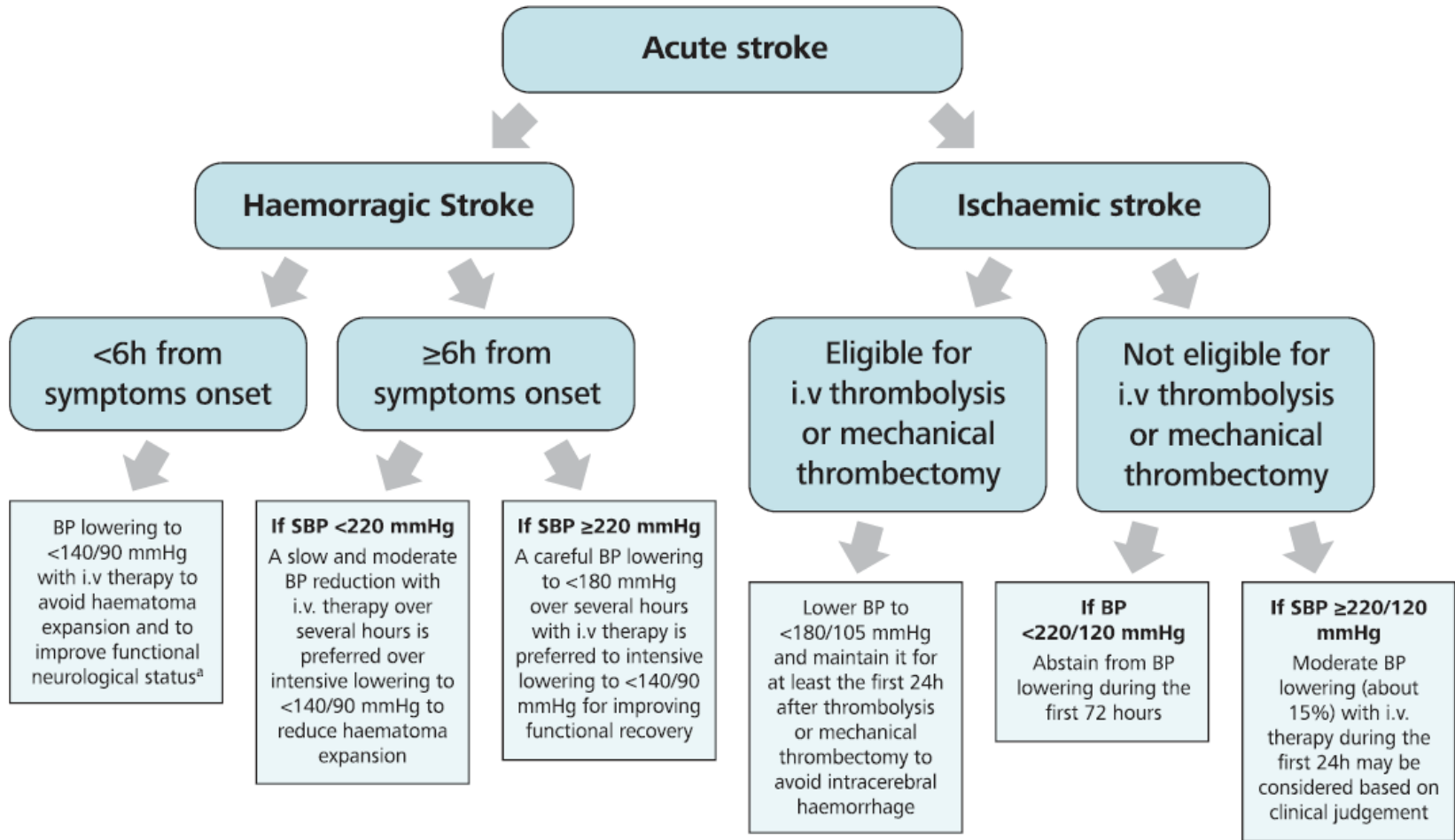


- ❖ At least 3 office BP measurements by auscultation (or automated oscillatory methods) to account for the varying BP values.
- ❖ Resting heart rate should be lowered < 110 BPM, targeting a heart rate < 80 BPM based on ECG analysis, particularly in symptomatic patients.

급성뇌졸중환자에서의 고혈압 조절

Recommendations and statements	CoR	LoE
In patients with haemorrhagic stroke and < 6h after symptom onset, a BP <140/90 mmHg is recommended to avoid haematoma expansion.	II	B
In patients with haemorrhagic stroke >6h after symptom onset, an SBP \geq 220 mmHg may be carefully lowered with i.v. therapy to <180 mmHg. If SBP < 220 mmHg, slow and moderate BP reductions are preferable over intensive BP to <140/90 mmHg.	II	B
In patients with acute ischemic stroke eligible for i.v. thrombolysis (IVT) or mechanical thrombectomy (MT), BP should be carefully lowered and maintained at <180/105 mmHg for at least the first 24 after intervention.	II	B
In patients not eligible for IVT or MT with BP \geq 220/120 mmHg, drug therapy may be considered based on clinical judgement, to reduce BP by 15% during the first 24 h after the stroke onset.	II	B
In patients with acute ischemic stroke Routine BP lowering with antihypertensive therapy is not recommended.	III	A

급성뇌졸중환자에서의 고혈압 조절



❖ Avoid absolute reductions of SBP >60 mmHg from initial SBP

당뇨병에서의 고혈압 조절

Non-dipping or elevated night-time BP are frequent in type 2 diabetes and should be monitored by ABPM or HBPM.	I	B
Antihypertensive treatment in type 2 diabetes is recommended to protect against macrovascular and microvascular complications.	I	A
Immediate lifestyle interventions and antihypertensive drug treatment are recommended for people with type 2 diabetes when office SBP is ≥ 140 mmHg and DBP is ≥ 90 mmHg.	I	A
Drug treatment strategies in patients with type 2 diabetes should be the same as for patients without diabetes but the primary aim is to lower BP below $<130/80$ mmHg	I	A
Well controlled, short-standing duration of the disease (< 10 yrs) with no evidence of HMOD and no additional CV risk factors categorized as being at moderate risk		
SGLT2is are recommended to reduce cardiac and kidney events in type 2 diabetes. These agents have a BP lowering effect.	I	A

만성콩팥병에서의 고혈압 조절

CKD stage 1 to 3
eGFR ≥ 30 ml/min/1.73 m²

ACEi or ARB + CCB
or T/TL Diuretic^a
Increase to full-dose if well tolerated^c

ACEi or ARB + CCB
+ T/TL Diuretic^a
Increase to full-dose if tolerated^c

True Resistant Hypertension^d
Add
I) **Spironolactone^e** (preferred)
or other **MRA^d**
or II) **BB^f** or **Alpha-1 Blocker**
or III) **Centrally acting agent**

+ SGLT2i or Finerenone^g

CKD stage 4 and 5 (not on dialysis)
eGFR < 30 ml/min/1.73 m²

ACEi^{b,c} or ARB^b + CCB
or Loop Diuretic
Increase to full-dose if well tolerated^c

ACEi^{b,c} or ARB^b + CCB
+ Loop Diuretic
Increase to full-dose if well tolerated^c

True Resistant Hypertension^d
Add
I) **Chlorthalidone** (preferred) or
other **T/TL Diuretic to Loop Diuretic**
or II) **BB^f** or **Alpha-1 Blocker**
or III) **Centrally acting agent**

Step 1

Dual combination

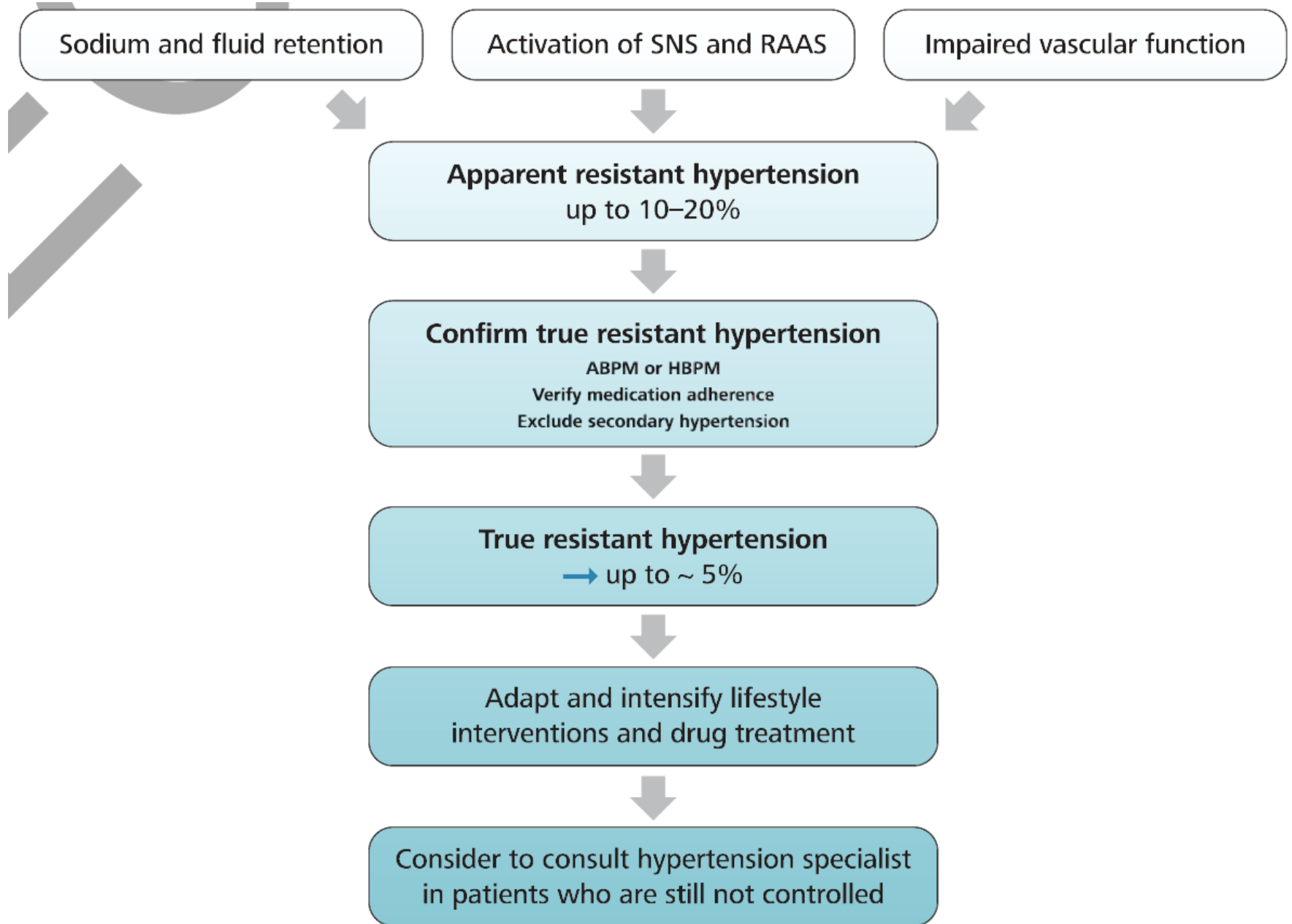
Step 2

Triple combination

Step 3

Add further drugs

저항성 고혈압 치료 총론



저항성 고혈압 치료 총론

Patients not controlled with
ACEi or ARB + CCB + Diuretic^b

CKD stage 1 to 3,
eGFR ≥ 30 ml/min/1.73 m²

- Add**
- I) **Spironolactone^d** (preferred)
or other **MRA^d**
 - or
 - II) **BB^e** or **Alpha1-blocker**
 - or
 - III) **Centrally acting agent**

CKD stage 4 and 5 (not on dialysis),
eGFR < 30 ml/min/1.73 m²

- Add^c**
- I) **Chlorthalidone** (preferred)
or other **T/TL Diuretic**
 - or
 - II) **BB^e** or **Alpha-1 Blocker**
 - or
 - III) **Centrally acting agent**

Consider Renal Denervation
If eGFR > 40 ml/min/1.73 m²

2차성 고혈압이 의심되는 경우

- ❖ **Younger patients (<40 years) with grade 2 or 3 HT** or HT 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
- ❖ **Hypertensive emergency**
- ❖ **Severe (grade 3) or malignant hypertension**
- ❖ Severe and/or extensive HMOD
- ❖ Clinical or biochemical features suggestive of endocrine causes of hypertension
- ❖ Clinical features suggestive of renovascular hypertension or fibromuscular dysplasia
- ❖ Clinical features suggestive of **obstructive sleep apnea**
- ❖ Severe hypertension in pregnancy (>160/110mmHg) or acute worsening of BP control in pregnant women with preexisting hypertension

대표적 2차성 고혈압: Primary aldosteronism

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

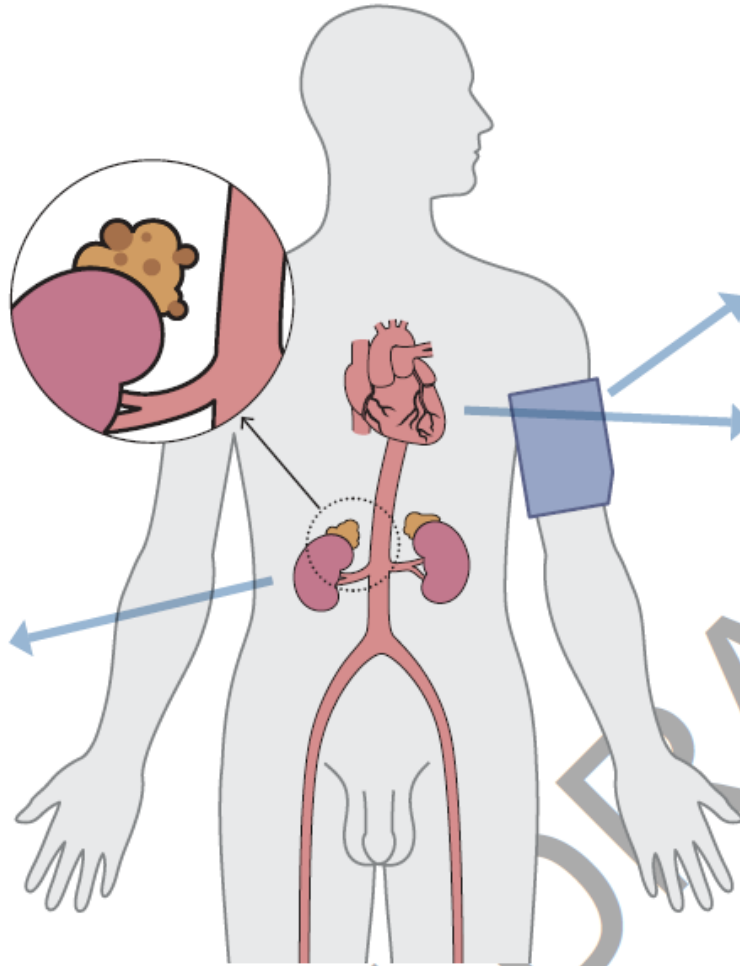
Plasma aldosterone to renin ratio (ARR)

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-reverse dipping

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

Increased CV Risk and mortality

대표적 2차성 고혈압: Atherosclerotic renovascular disease

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 CT or MR-angiography

Further work-up

Angio-CT or angio-MR

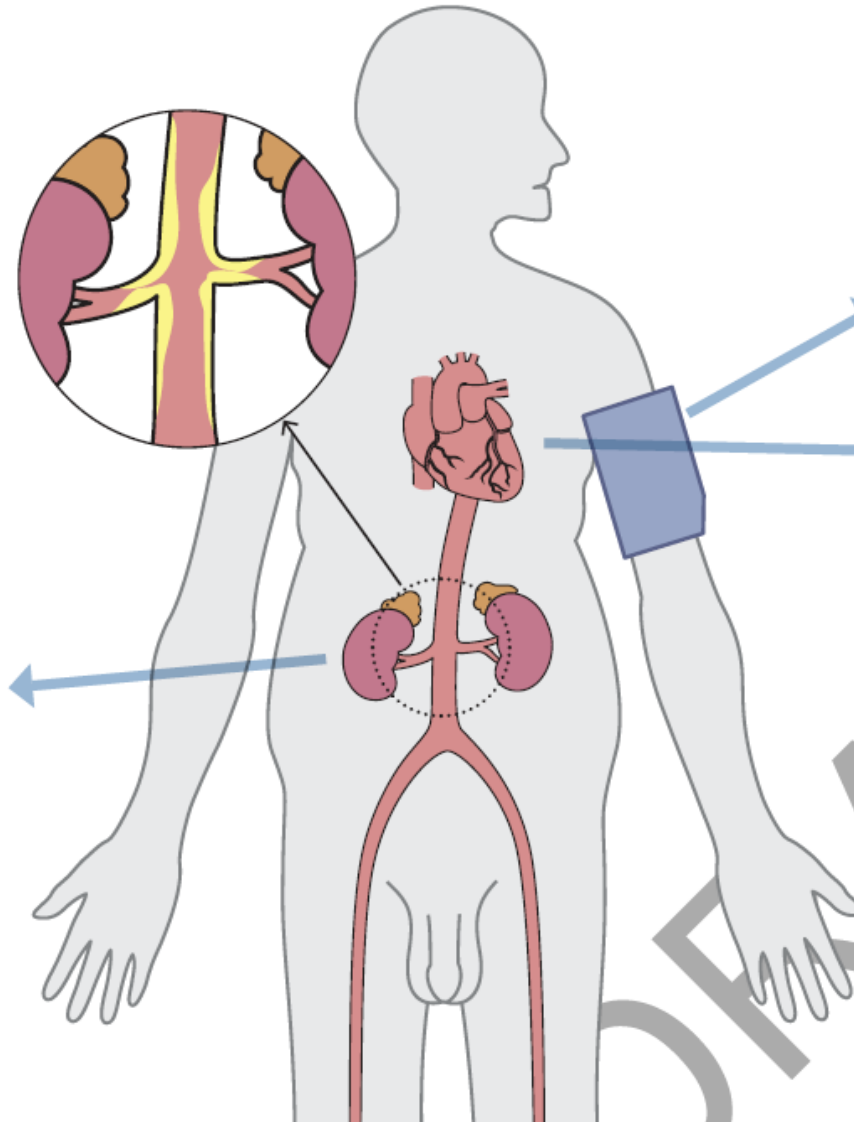
Invasive catheter angiography

Treatment^{c,d}

Antihypertensive treatment

Strict control of CV risk factors

Revascularization (selected cases)



Cardiovascular phenotype

24h ABPM – resistant hypertension, frequent non-reverse dipping

- LVH
- Decreased diastolic function
- Decreased systolic function

Increased CV Risk and mortality

대표적 2차성 고혈압: Fibromuscular Dysplasia

Prevalence:
<1 to 6%^a

Suggestive symptoms, signs and findings

Early-onset/ severe hypertension
Migraine
Pulsatile tinnitus

1st choice screening test^b

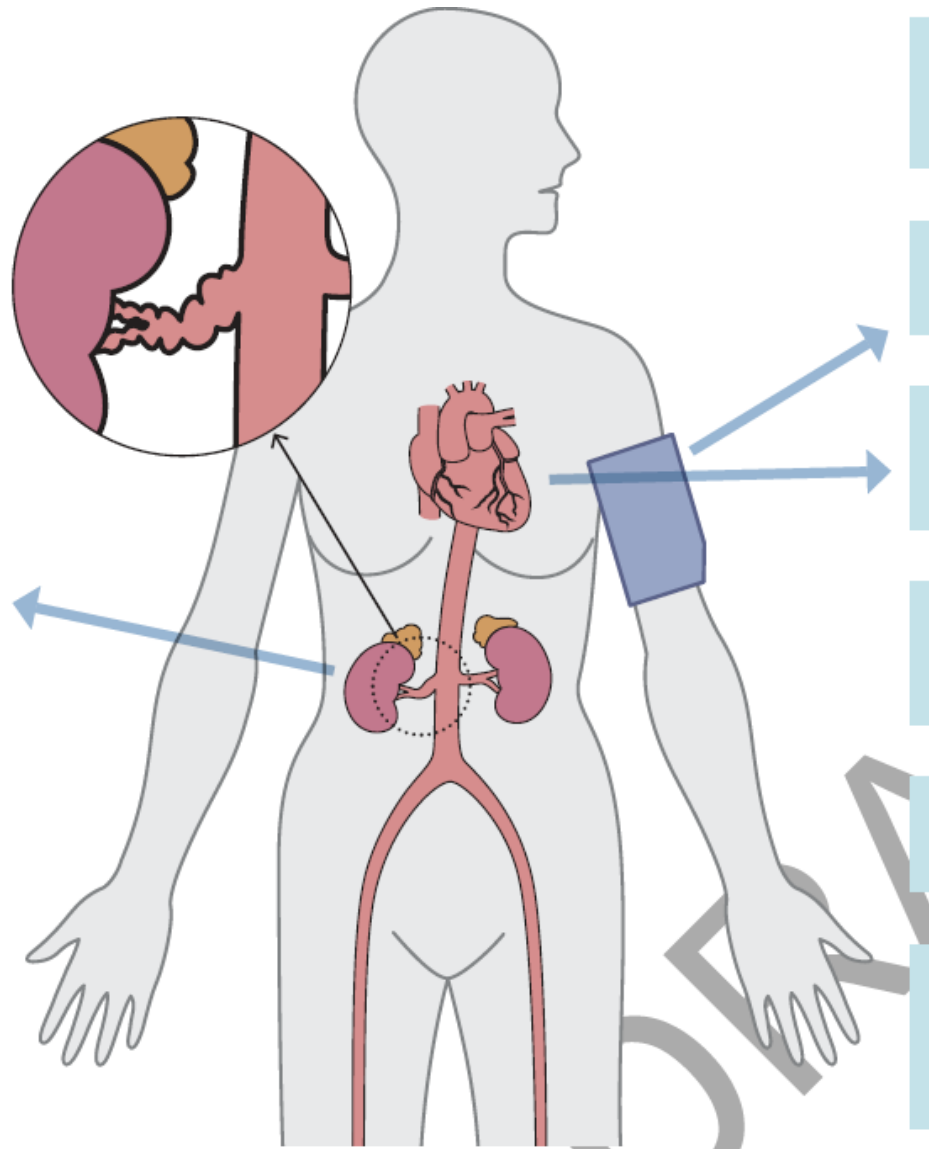
Renal artery duplex ultrasound;
otherwise CT or MR-angiography

Treatment

Antihypertensive treatment
Angioplasty without stenting^{c,d}

Follow-up

- Whole body CT- or MR-angiography 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

대표적 2차성 고혈압: Pheochromocytoma / paraganglioma

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 enhanced CT or MRI

Functional imaging

Genetic testing^c

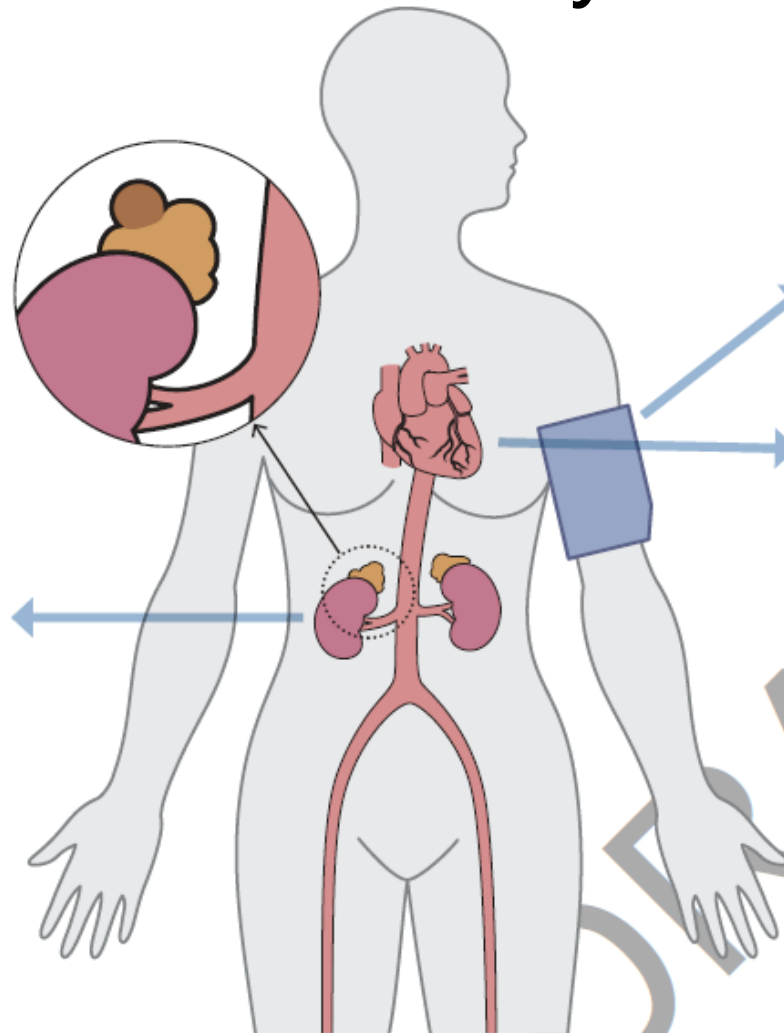
Treatment^d

Surgical resection

(Pheochromocytoma: minimally invasive laparoscopic adrenalectomy)

Follow-up^e

In most cases > 10 yrs



Cardiovascular phenotype

24h ABPM – frequent non-reverse dipping

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

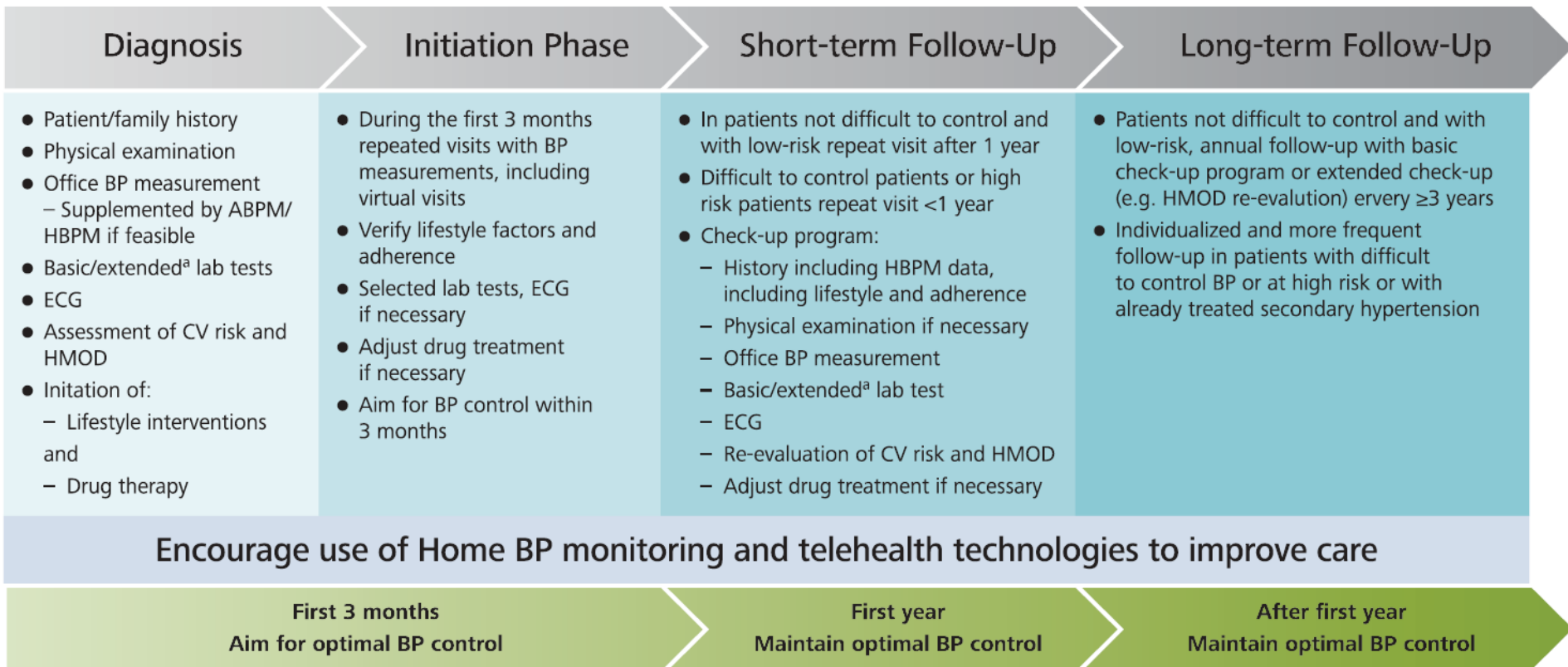
Increased CV Risk and mortality

고혈압 응급 치료가 필요한 경우와 선택 약제

- ❖ Malignant hypertension is also known as a HT crisis
 - ✓ Hypertensive emergency is when a rise in BP occurs with signs of organ damage. This is a medical emergency that requires immediate care.
 - ✓ Hypertensive urgency occurs when BP is abnormally high, but there are no signs of organ damage.

Clinical presentation	Timing and BP target	First-line treatment	Alternative
Malignant hypertension with or without acute renal failure	Several hours Reduce MAP by 20–25%	Labetalol ^a Nicardipine	Nitroprusside Urapidil
Hypertensive encephalopathy	Immediately reduce MAP by 20–25%	Labetalol ^a Nicardipine	Nitroprusside
Acute coronary event	Immediate reduce SBP to <140 mmHg	Nitroglycerine Labetalol ^a	Urapidil
Acute cardiogenic pulmonary edema	Immediately reduce SBP to <140 mmHg	Nitroprusside or nitroglycerine (with loop diuretic)	Urapidil (with loop diuretic)
Acute aortic dissection	Immediately reduce SBP to <120 mmHg and heart rate to <60 bpm	Esmolol AND nitroprusside or nitroglycerine or nicardipine	Labetalol ^a or metoprolol
Eclampsia and severe preeclampsia/HELLP	Immediately reduce SBP to <160 mmHg and DBP to <105 mmHg	Labetalol ^a or nicardipine and magnesium sulphate	Consider delivery

환자 약제 치료 간격



2023 ESH Guideline Updates Summary

- General BP target : 140/80mmHg (Not < 120/70 mmHg)
 - Elderly(65-79 yrs): 140/80mmHg (130/80mmHg if well tolerated)
 - Non-frail, Very Elderly(≥ 80 yrs): <150/80mmHg(SBP 140mmHg if well tolerated)
 - Frail patients : Individual Therapy
- Resistant Hypertension: 140/90mmHg(130/80mmHg if well tolerated)
- DM with HTN : 130/80mmHg
- CKD with HTN : 130/80mmHg (Not < 120/70 mmHg)
- Diuretics : CV Prevention에 있어 Thiazide & Thiazide-like diuretics 동등하게 권고 (DCP Trial 반영)