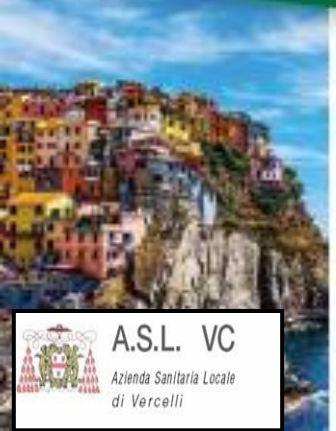
TERAPIA DI ASSOCIAZIONE

EVENTO FORMATIVO
INTERREGIONALE SIIA
PIEMONTE
LIGURIA
VALLE D'AOSTA
Torino, 12 ottobre 2024

NELL'IPERTENSIONE DI DIFFICILE CONTROLLO



Erica Delsignore
S.C. Medicina Interna-
Ospedale S. Andrea - Vercelli

A.S.L. VC
Azienda Sanitaria Locale
di Vercelli

SIG. L. 62 ANNI

- Anamnesi famigliare: ictus cerebri, cardiopatia ischemica; 3 figli in abs
- Anamnesi fisiologica: sviluppo psicofisico nella norma
- elettricista, fuma circa 5-6 sigarette/ die (in precedenza fino a 20-25/die), vino occasionalmente, 2 caffè/die. Russamento notturno

- **A.P.R:** BPCO con periodiche riacutizzazioni in tabagismo.
- Sovrappeso (prima obesità stadio I). Dislipidemia mista.
- Diabete mellito tipo 2 in regime dietetico da 8 aa.
- Ipertensione arteriosa da alcuni aa (avviati e autosospesi numerosi farmaci per EAs, astenia, inefficacia…)
- Da 1 anno **doxazosin 4 mg 1 cp → 1 x 2**

- per episodi di tachicardia E PA non controllata **aggiunto bisoprololo 5 mg**

- Per scarso controllo pressorio **Aggiunta clonidina TTS1/settimana**

- **A.P.P.** dopo autosospensione di clonidina , accesso al DEA puntata ipertensiva→ PA 200/110 mmHg con flushing e tachicardia fc 110/min: trattato con clonidina 1 fl im , **dimesso con PA 168/93 mmHg e ripresa di clonidina cerotto**

- Richiesta di visita del MMG: **ipertensione resistente e puntate ipertensive**

- Peso 83 Kg; h 168 cm; BMI 29,7
- PA 160 /85 braccio dx; PA 165/90 mmHg braccio sx
- in clinostatismo PA 165/100 PA , in ortostatismo PA 150/90 mmHg

- toni cardiaci validi, ritmici, fc 72/min soffio sistolico 2/6
- torace: MV ridotto ed aspro su tutto l'ambito
- non edemi declivi, non soffi arteriosi
- Addome non dolorabile, organi nei limiti
- **Aree di eritema nelle zone di applicazione cerotto**

Terapia in atto: Umeclidinio /vilanterolo 55/22 mcg 1 inalaz/die, doxazosin 4 mg x 2, clonidina TTS 1 /settimana, bisoprololo 5 mg 1 cp (SOSPESO DA CIRCA 2 SETTIMANE..)

- *Aderenza terapeutica: Percentuale di dosi del farmaco assunte così come prescritte*

Varia dal 50% per la prevenzione primaria di ASCVD al 66% per la prevenzione secondaria.

Circa il 9% dei casi di ASCVD in Europa può essere attribuito alla scarsa aderenza ai farmaci.

- *Persistenza: intervallo di tempo tra l'inizio di una terapia e la sua interruzione*

Visseren, 2021 ESC Guidelines on CVD Prevention

NON ADERENZA COME CAUSA DI ACCESSO AL PS

Accessi in P.S. riconducibili all'ipertensione arteriosa sono frequenti, con occupazione del posto letto in area critica e anche notevole impiego di risorse economico-sanitarie per accertamenti diagnostici e ottimizzazione terapeutica.

- Fattori predittivi: sesso femminile, obesità, presenza di cardiopatia ipertensiva o ischemica, impiego di terapie farmacologiche complesse (politerapia) e abuso di sostanze stimolanti o di FANS o cortisonici
- Uno studio (10/2014-06/2015) ha identificato come fattore potenzialmente coinvolto nelle urgenze /emergenze HT la mancata aderenza terapeutica: su 100 pz l'84% aveva urgenza HT (con media PA 200/105 mmHg), solo il 16% emergenza.
- L'86% dichiarava di essere in trattamento e quasi tutti i pz di essere aderenti, ma tra i pz su cui è stato eseguito dosaggio dei metaboliti urinari (62) il 24% è risultato NON aderente e il 36% parzialmente aderente alla terapia.
- Fattori correlati alla non aderenza: storia di ipertensione di più lunga data, un numero maggiore di compresse ed un numero maggiore di farmaci.

Wallbach J Clin Hypertens (Greenwich) 2019

CONSEGUENZE DELLA NON ADERENZA NELLA TERAPIA ANTIHT

•Small increases in BP havemajor clinical implications on a population basis, Because a 2 mmHg rise in systolic BP is associated with a 7% and 10% increased risk of mortality from ischaemic heart disease and stroke, respectively· (Turtle, Br J Clin Pharmacol 2012)

- Una maggiore aderenza ai farmaci per condizioni croniche come ipertensione, diabete mellito, ipercolesterolemia e insufficienza cardiaca è stata associata a costi immediati più elevati per spesa farmaci, ma a minori costi medici non farmacologici, ottenendo una riduzione complessiva netta dei costi sanitari
- (Ho et al Medication Adherence, *Circulation* 2009)

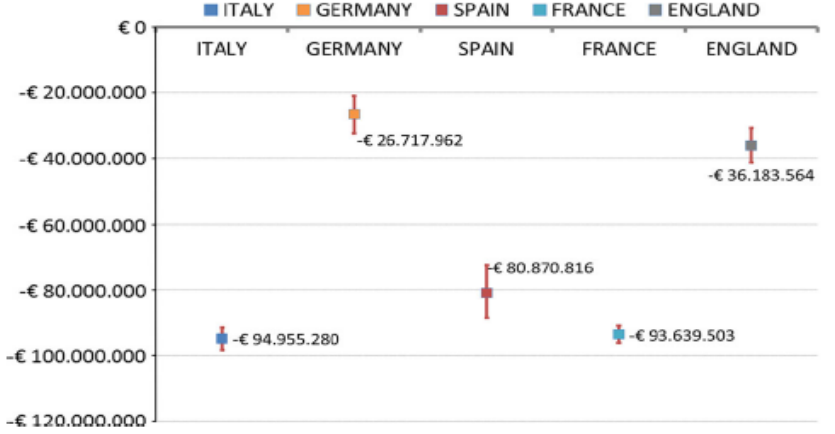


Fig. 2 Estimation of costs avoided due to an increase in adherence (Scenario 1–Scenario 2)—average and CI 95 %

8,6M (1,4 in Italia, 3,3 in Germania, 1,2 in Spagna, 1,8 in Francia e 0·9 in Inghilterra) di eventi CV stimati correlati all'ipertensione nell'Orizzonte temporale di 10 aa· <u>Aumentare l'aderenza agli antiHT al 70% farebbe risparmiare un tot· di € 332M</u>

Mennini, Eur J Health Econ (2015)

TABLE 9. Assessment of hypertension-mediated organ damage (HMOD)[a]

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 [illegible]	Detect and classify CKD
Ser[illegible]	[illegible] d cla[illegible]
Ext[illegible]	
Echocardiography	Evaluate structure and function of t[illegible] diameter and ascending aortic an[illegible]
	[illegible] uate a[illegible]
	[illegible] ermine[illegible]
	[illegible] ermine[illegible]
	[illegible] en for[illegible]
Kidney ultrasound	Evaluate s[illegible] ultrasonography)
Spectral doppler ultrasonography	Diagnosis of renovascular disease and determination[illegible]
ABI	Screen for LEAD
Retina microvasculature	[illegible]
Cognitive function testing (MMSE, MoCA)	Screen for early stages of dementia
Brain imaging (CT, MRI)	Detect structural brain damage

ECG: RS a 66/min, SVS

microalbuminuria 145,7 mg/g creatinina

creatinina 1,3 mg/dl, GFR 69, Na 135, K+ 3,9

Test ergometrico (2022): negativo per ischemie inducibili da sforzo

ipertrofia concentrica (121 g/m2), FE 59%, A sx dilatato, disfunz diastolica

Doppler TSA: ateromasia carotidi comune ed interna bilateralmente senza placche o stenosi emodinamiche. IMT 1,2

Eco addome: fegato steatosico, reni di normali dimensioni, con spessore corticale conservato, lievemente iperriflettente, aorta di diametro nei limiti con qualche calcificazione parietale

ABI 1.1

GLICEMIA 104 MG/DL, HbAa1C 50 mmol/mol, TSH r2,3

2023 ESH Guidelines

COPD AND COMORBIDITIES

KEY POINTS:

- COPD often coexists with other diseases (comorbidities) that may have a significant impact on disease course.
- In general, the presence of comorbidities should not alter COPD treatment and comorbidities should be treated per usual standards regardless of the presence of COPD.

- **Cardiovascular diseases (CVD)**
- **Heart failure**
- **Ischaemic heart disease (IHD)**
- **Arrhythmias**
- **Peripheral vascular disease**
- **Hypertension**
- **Lung cancer**

GOLD Grades and Severity of Airflow Obstruction in COPD (based on post-bronchodilator FEV1)

Table 2.6

In COPD patients (FEV1/FVC < 0.7):

GOLD 1:	Mild	FEV1 ≥ 80% predicted
GOLD 2:	Moderate	50% ≤ FEV1 < 80% predicted
GOLD 3:	Severe	30% ≤ FEV1 < 50% predicted
GOLD 4:	Very Severe	FEV1 < 30% predicted

Initial Pharmacological Treatment

≥2 moderate exacerbations or ≥1 leading to hospitalization	GROUP E: LABA + LAMA* *consider LABA + LAMA + ICS* if blood eos ≥ 300*	
0 or 1 moderate exacerbations (not leading to hospital admission)	GROUP A: A bronchodilator	GROUP B: LABA + LAMA*
	mMRC 0–1, CAT <10	mMRC ≥2, CAT ≥10

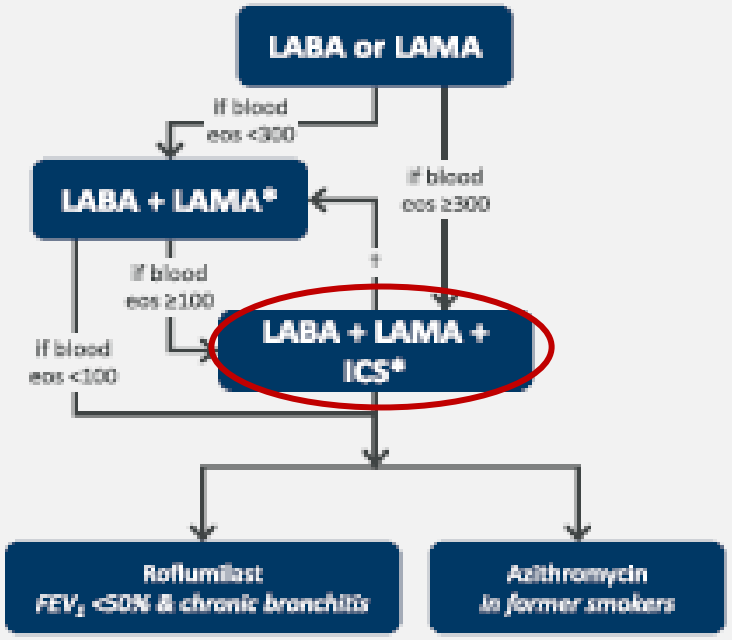
Modified MRC Dyspnea Scale

Table 2.7

PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

mMRC Grade 0	mMRC Grade 1	mMRC Grade 2	mMRC Grade 3	mMRC Grade 4
I only get breathless with strenuous exercise	I get short of breath when hurrying on the level or walking up a slight hill	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level	I stop for breath after walking about 100 meters or after a few minutes on the level	I am too breathless to leave the house or I am breathless when dressing or undressing
☐	✗	✗	☐	☐

EXACERBATIONS

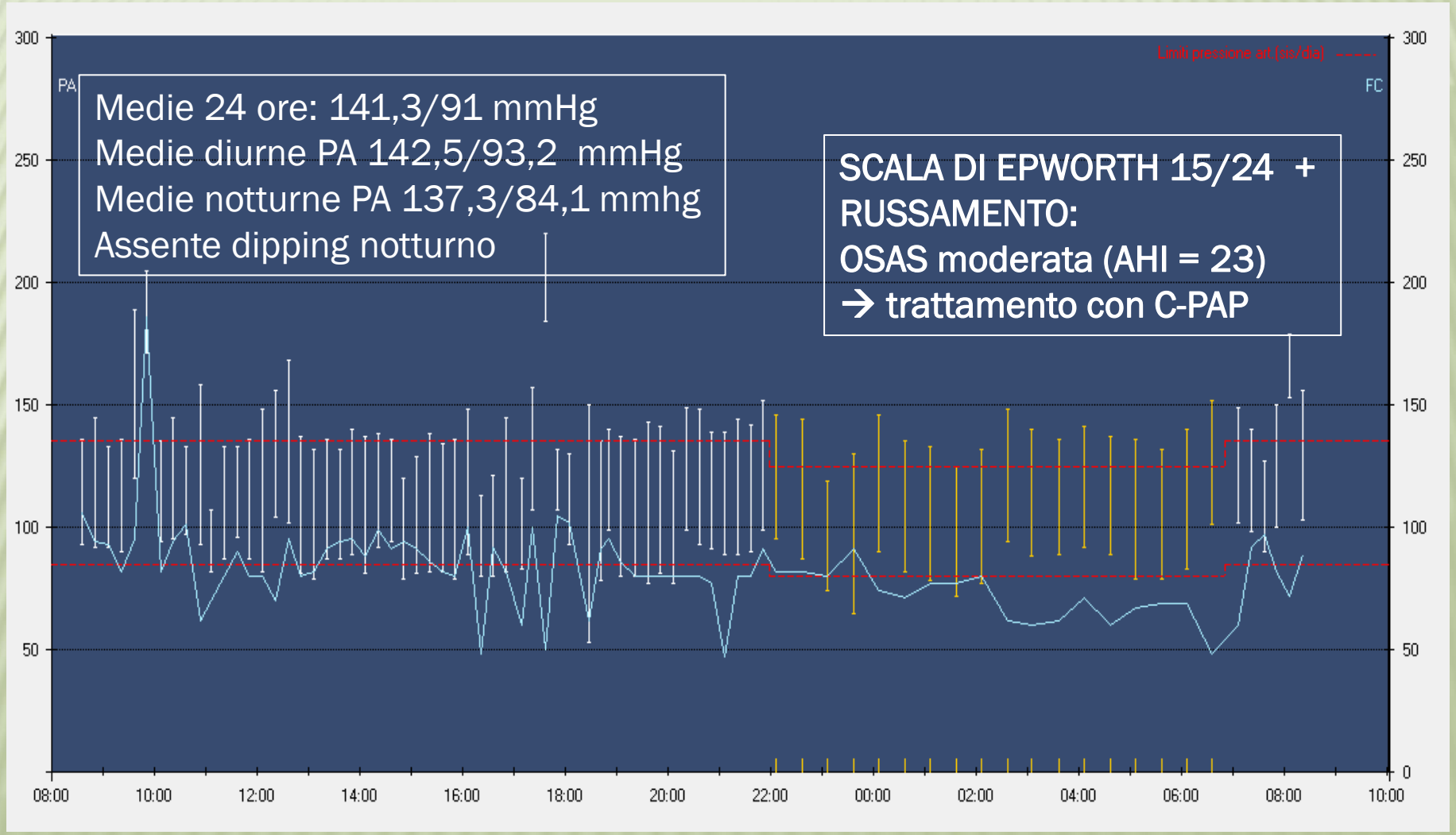


Uomo, 62 aa, Fumatore
Colest tot 242, HDL 37 mg/dl, LDL 176, TG 215 mg/dl, colest non HDL 205 mg/dl
PAs 165/85 mmHg

Patients with type 2 diabetes mellitus			
Patients with type 1 DM above 40 years of age may also be classified according to these criteria	Patients with well controlled short-standing DM (e.g. <10 years), no evidence of TOD and no additional ASCVD risk factors	**Moderate-risk**	N/A
	Patients with DM without ASCVD and/or severe TOD, and not fulfilling the moderate risk criteria.	**High-risk**	Residual 10-year CVD risk estimation after general prevention goals (e.g. with the ADVANCE risk score or DIAL model). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. DIAL model).
	Patients with DM with established ASCVD and/or severe TOD:[87,93-95] • eGFR <45 mL/min/1.73 m^2 irrespective of albuminuria • eGFR 45-59 mL/min/1.73 m^2 and microalbuminuria (ACR 30 -300 mg/g) • Proteinuria (ACR >300 mg/g) • Presence of microvascular disease in at least 3 different sites (e.g. microalbuminuria plus retinopathy plus neuropathy)	**Very high-risk**	Residual 10-year CVD risk estimation after general prevention goals (e.g. with the SMART risk score for established CVD or with the ADVANCE risk score or with the DIAL model). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. DIAL model).

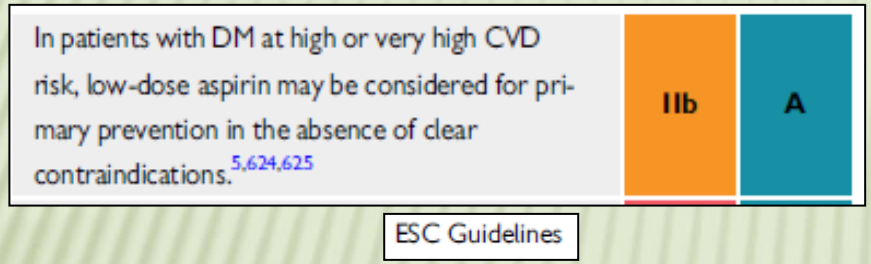
2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

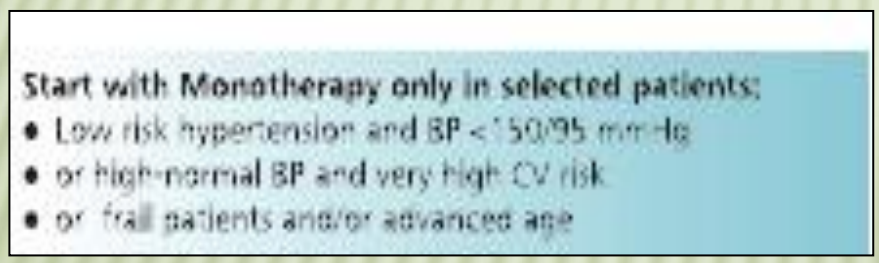
ABPM 1

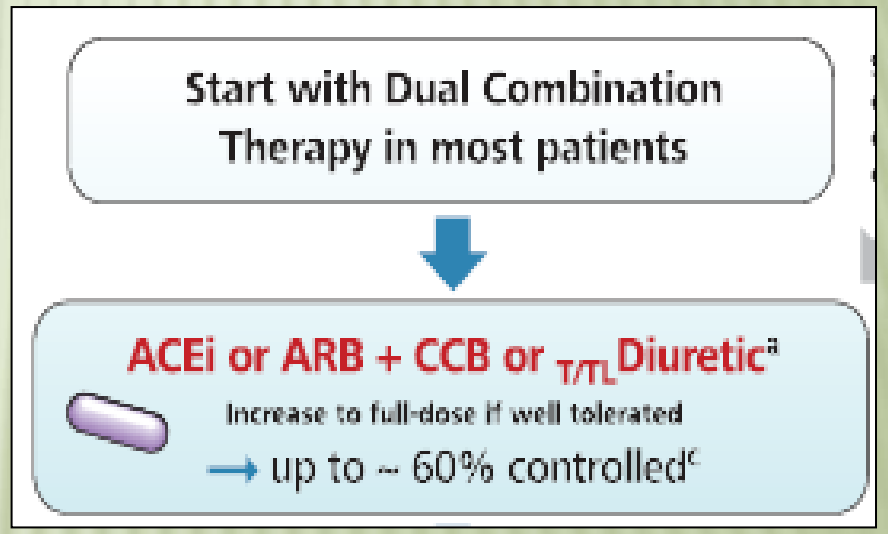

Limiti pressione art (sis/dia)
PA
FC
Medie 24 ore: 141,3/91 mmHg
Medie diurne PA 142,5/93,2 mmHg
Medie notturne PA 137,3/84,1 mmhg
Assente dipping notturno
SCALA DI EPWORTH 15/24 +
RUSSAMENTO:
OSAS moderata (AHI = 23)
→ trattamento con C-PAP
300
250
200
150
100
50
0
08:00
10:00
12:00
14:00
16:00
18:00
20:00
22:00
00:00
02:00
04:00
06:00
08:00
10:00

- Si consiglia:

  - mantenere sospeso beta bloccante
  - stop graduale di clonidina
  - stop doxazosin
  - stop fumo + attività fisica + calo ponderale





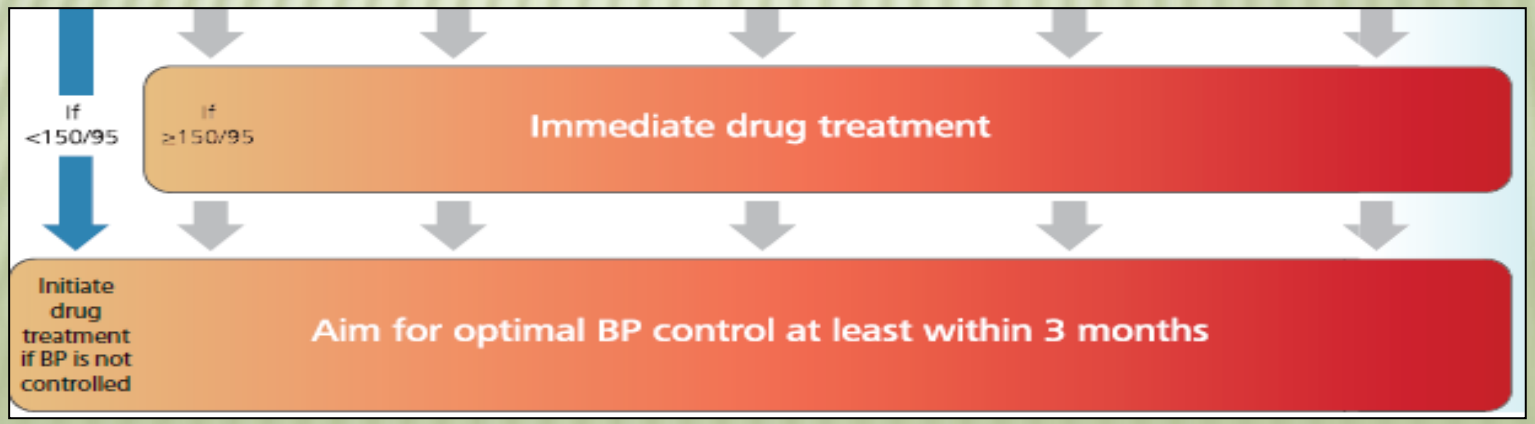


- avviare perindopril/indapamide 10/2,5 mg

- controllo a circa 1 mese con esami, HBPM e ABPM

3 MESI DOPO: VISITA DI CONTROLLO

- Sospensione di BB e clonidina senza problemi ma…
- Sospeso anche ACE/diuretico per comparsa di tosse
- Avviata nifedipina crono 60 mg → <u>modesti edemi declivi</u> → aggiunta di fusorsemide 25 mg (non efficace) → autosospensione
- Ha ripreso(o ha mantenuto??) invece doxazosin 4 mg
- PA 160/95 mmHg



ADHERENCE AND PERSISTENCE WITH ANTIHYPERTENSIVE REGIMENS

Table II. Persistence With Antihypertensive Medication Over Time by Drug Class

Study	No.	Persistence Rate (%)				
		Diuretic	β-Blocker	CCB	ACEI	ARB
1 Year						
Bloom 1998[42]	21,723	38	43	50	58	64
Conlin 2001[39]	15,175	21	46	54	61	67
Hasford 2002[21]	2,416	34	50	44	42	51
Bourgault 2005[17]	21,326	45	50	55	59	66
Erkens 2005[43]	2,243	33	35	35	60	62
Perreault 2005[18]	14,947	61	68	68	71	73
Hoer 2007[37]	62,745	26	14	34	34	53
Patel 2007[44]	242,882	30	40	38	48	52
Elliott 2007[45]	60,685	56	–	60	65	69
3 Years						
Bourgault 2005[17]	21,326	29	34	38	40	53
Hasford 2007[38]	13,763	9	13	12	14	11
Perreault 2005[17]	21,011	48	57	58	58	59
4 Years						
Burke 2006[41]	109,454	31	33	35	40	42
Conlin 2001[39]	15,175	16	35	41	46	51

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker.

Elliot, J Clin Hypertens (Greenwich), 2009

Incidence of cough associated with ACEI between 3.9% and 35%. *J Clin Hypertens.* 2023

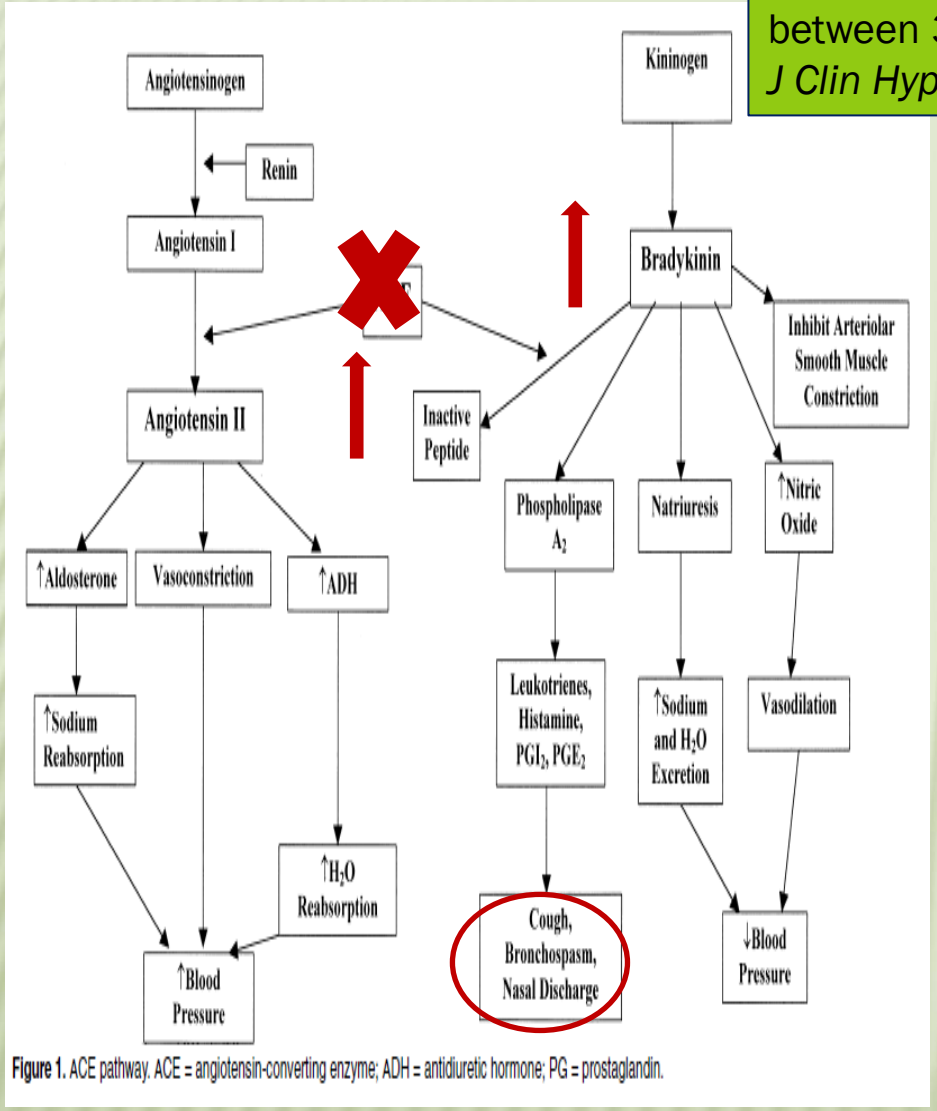


Figure 1. ACE pathway. ACE = angiotensin-converting enzyme; ADH = antidiuretic hormone; PG = prostaglandin.

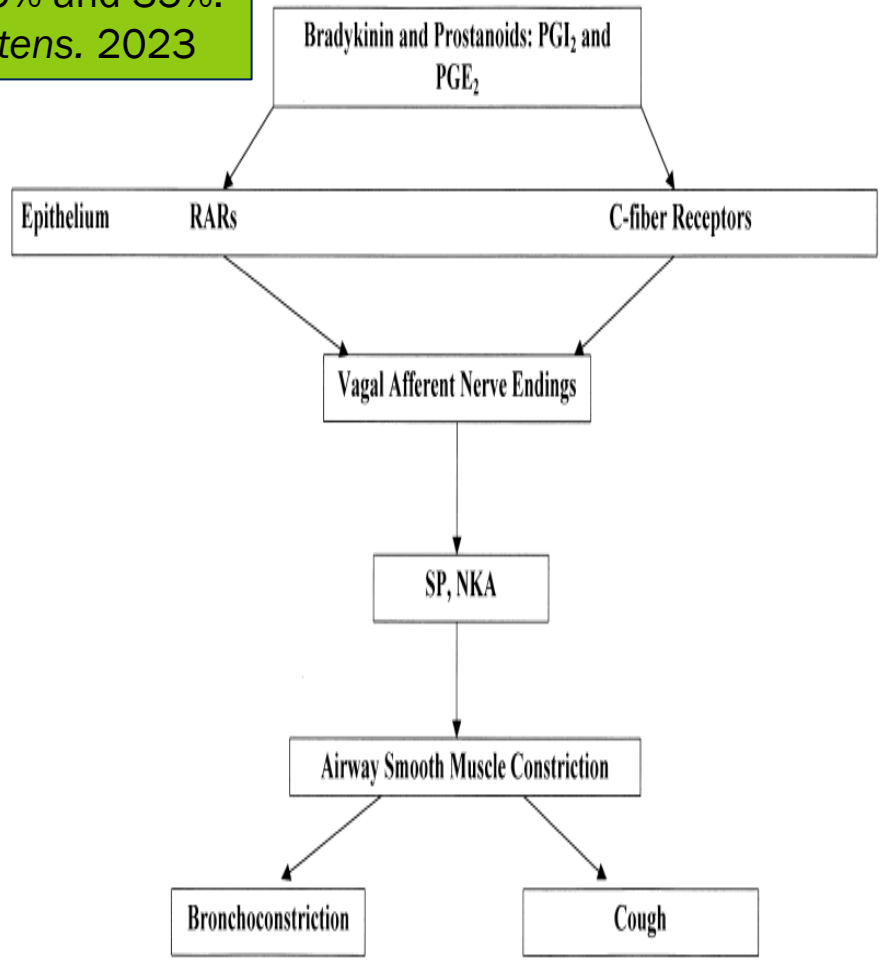
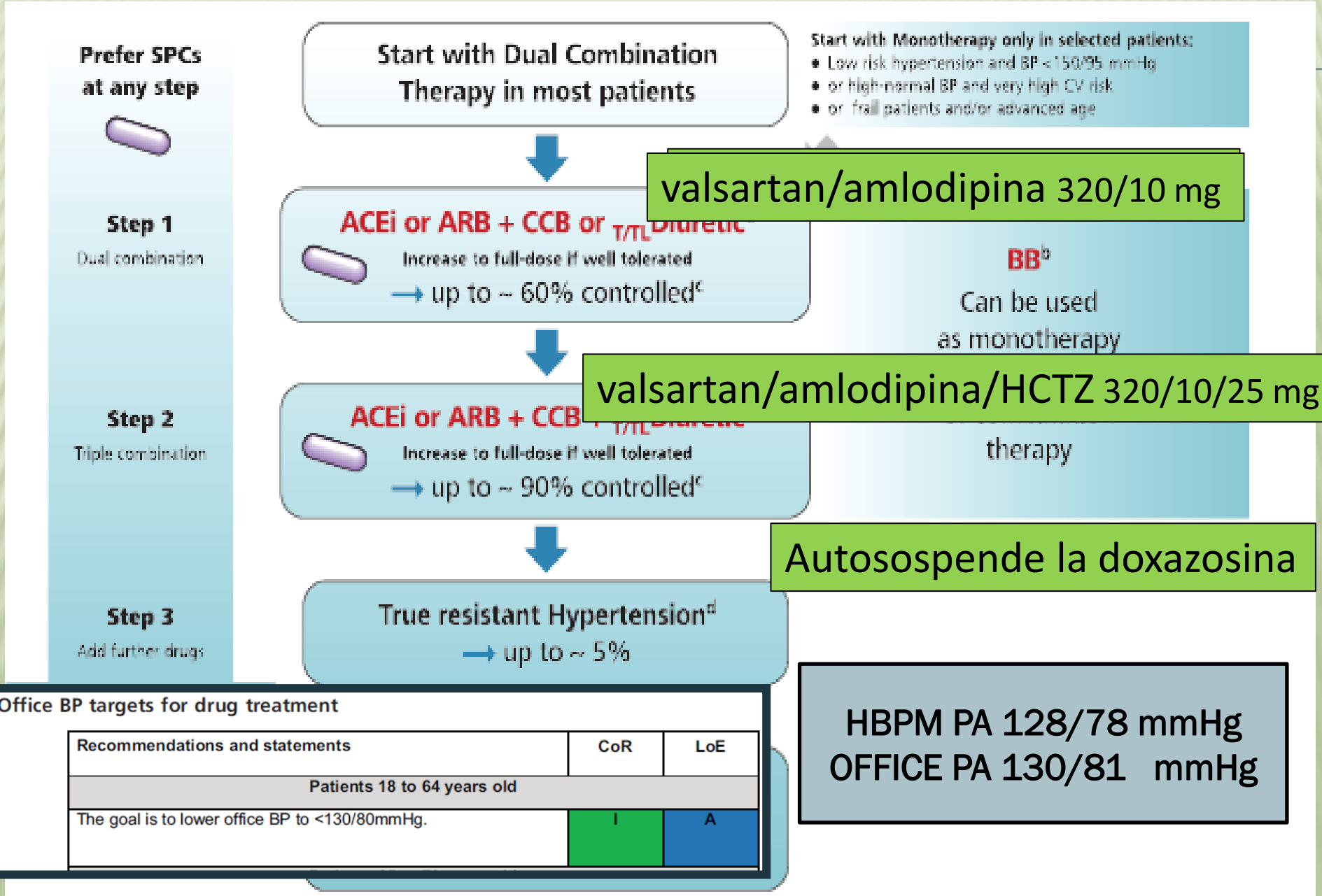
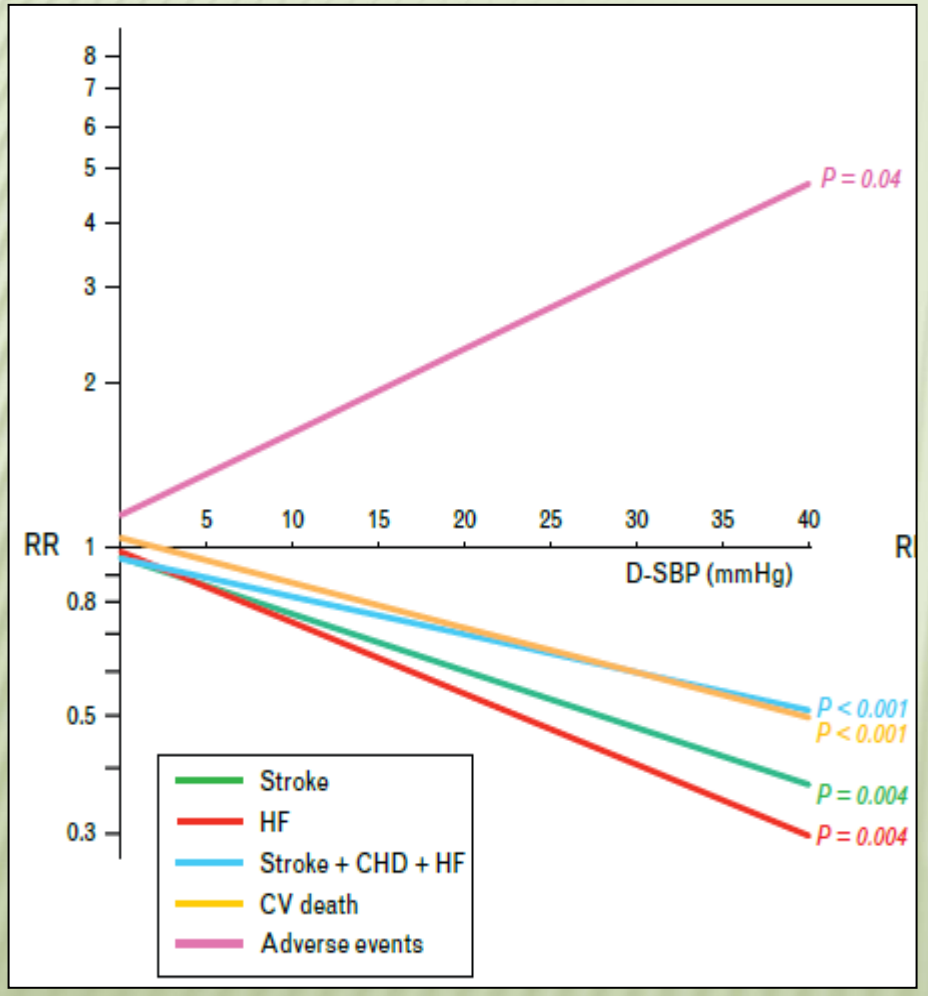


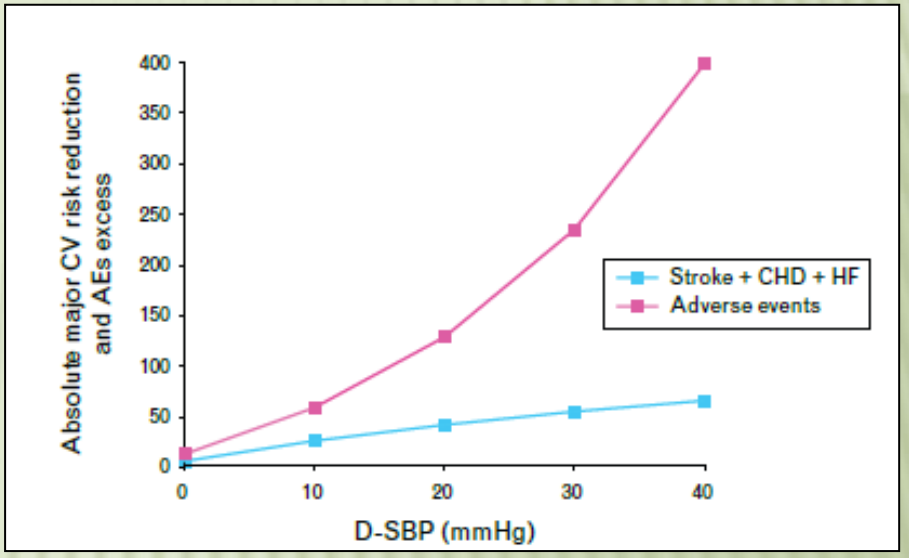
Figure 2. ACE inhibitor–associated pulmonary dysfunction. ACE = angiotensin-converting enzyme; NKA = neurokinin A; PG = prostaglandin; RARs = rapidly adapting stretch receptors; SP = substance P.

Packard, Ann Pharmacother 2002


Prefer SPCs at any step
Start with Dual Combination Therapy in most patients
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
Step 1
Dual combination
ACEi or ARB + CCB or T/TL Diuretic
Increase to full-dose if well tolerated
→ up to ~ 60% controlled[c]
valsartan/amlodipina 320/10 mg
BB[b]
Can be used as monotherapy
Step 2
Triple combination
ACEi or ARB + CCB + T/TL Diuretic
Increase to full-dose if well tolerated
→ up to ~ 90% controlled[c]
valsartan/amlodipina/HCTZ 320/10/25 mg
therapy
Autosospende la doxazosina
Step 3
Add further drugs
True resistant Hypertension[d]
→ up to ~ 5%
Office BP targets for drug treatment
Recommendations and statements
CoR
LoE
Patients 18 to 64 years old
The goal is to lower office BP to <130/80mmHg.
I
A
HBPM PA 128/78 mmHg
OFFICE PA 130/81 mmHg

Effects of blood pressure lowering treatment in hypertension: 8. Outcome reductions vs. discontinuations because of adverse drug events – meta-analyses of randomized trials





Sum of withdrawals due to hypotension or dizziness, worsening renal function (endpoint not reached), hyperkalemia, allergic reaction, cough, peripheral edema, insufficient diabetes control, worsening renal function, gastrointestinal disturbances, headache, nausea, fatigue, …

Thomopulos, Journal of Hypertension 2016

E' IPERTENSIONE RESISTENTE?

- Hypertension is defined as resistant when a treatment strategy including appropriate lifestyle measures and treatment with maximum or maximally tolerated doses of a diuretic (thiazide or thiazide-like), a RAS blocker, and a calcium channel blocker fail to lower office systolic and diastolic BP values to <140 mmHg and/or <90 mmHg, respectively. These uncontrolled BP values must be confirmed by out-of-office BP measurements

2024 ESC Guidelines

Ipertensione di difficile controllo:

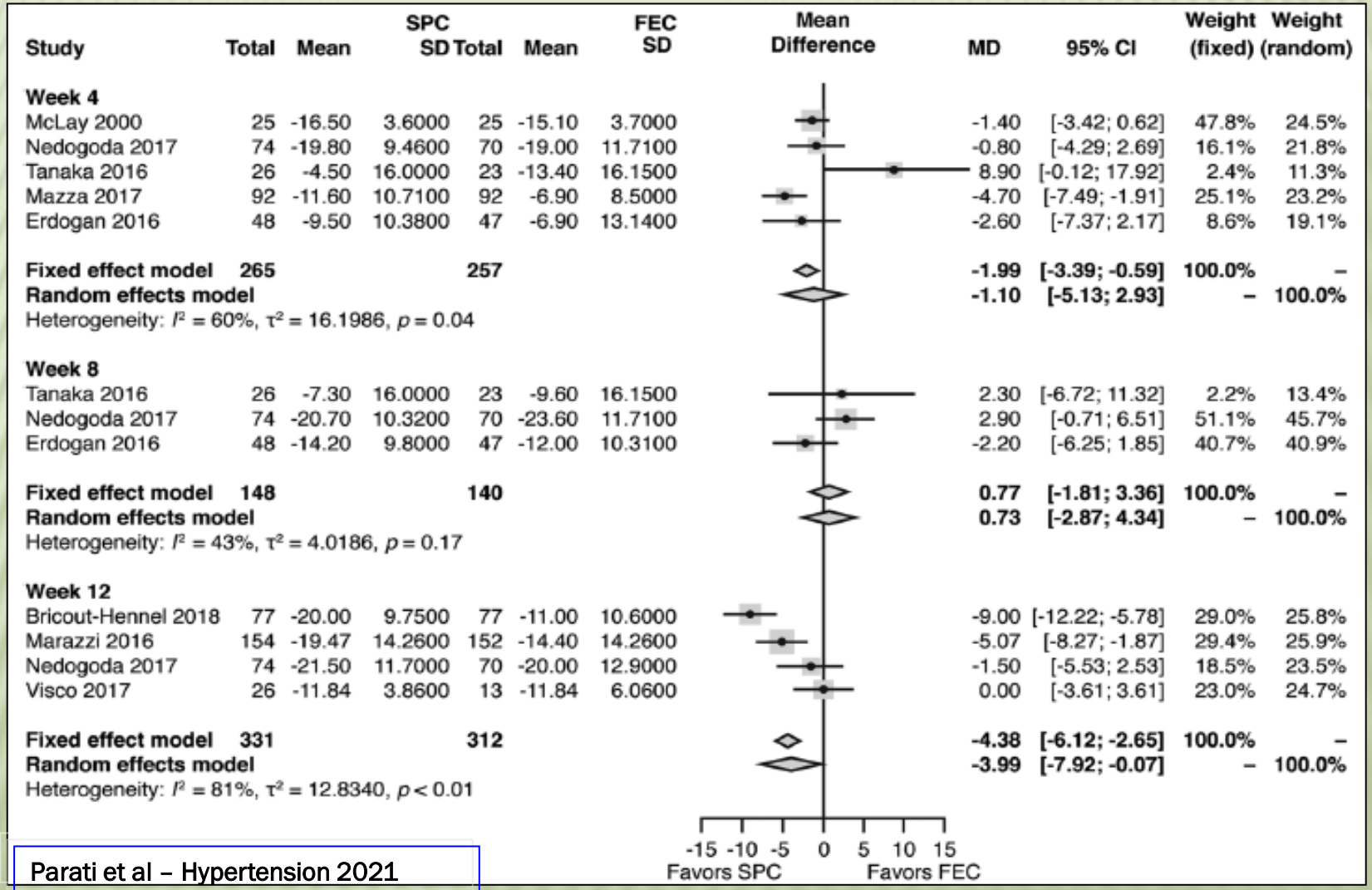
- **ipertensione resistente**
- **Condizioni patologiche associate (IRC, obesità, DM, OSAS)**
- **Stile di vita non adeguato**
- **Mancata aderenza terapeutica**

Visco et al, J of Human Hypert 2018

- the process of care in these cases should be patient-centered we recommend that the concept of *difficult-to-treat hypertension* is abandoned in favor of the concept of the *difficult-to-treat patient*…
- *difficult-to-treat* patient does not necessarily correspond exactly to the *resistant hypertensive* patient….

Bruno et al, High Blood Pressure & Cardiovascular Prevention (2020)

Single pill vs free-equivalent combination therapy



Parati et al – Hypertension 2021

Relative reduction in blood pressure (BP): single-pill combination (SPC) therapy vs free-equivalent combination therapy.

Main studies that support a beneficial effect of RAS blockers in COPD patients.

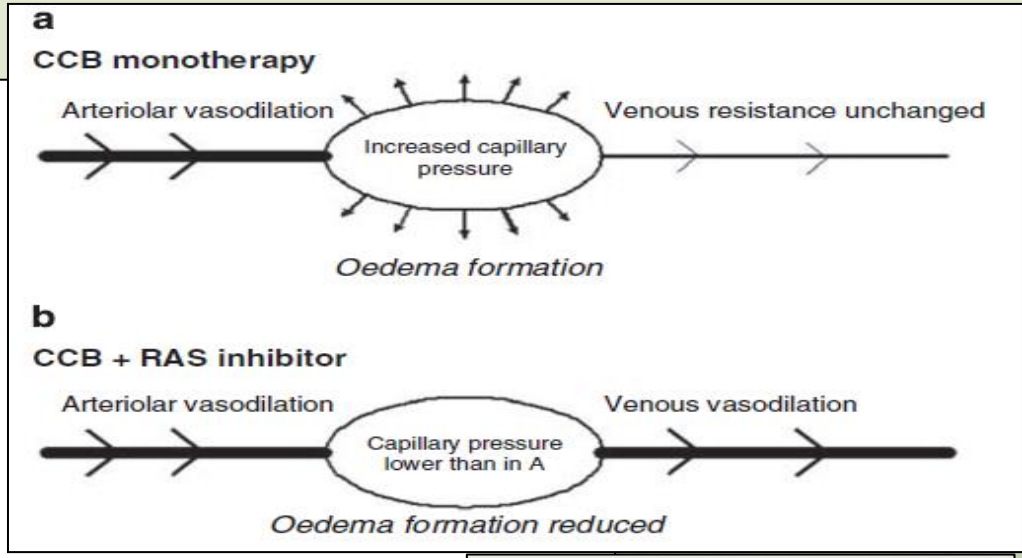
Author (year)	No. of pts	Type of study	Results/findings
Mancini et al. [77] (2006)	5853	Retrospective	Either ACEi or ARBs and statins reduced both cardiovascular and pulmonary outcomes, with the largest benefits occurring with the combination of these drugs. This combination was associated with a reduction in COPD hospitalization (RR 0.66, 95% CI 0.51 to 0.85) and total mortality (RR 0.42, 95% CI 0.33 to 0.52) not only in the high cardiovascular risk cohort but also in the low cardiovascular risk cohort (RR 0.77, 95% CI 0.67 to 0.87, and RR 0.36, 95% CI 0.28 to 0.45, respectively)
Mortensen et al. [78] (2009)	11 212	Retrospective	ACEi/ARB use (0.55, 95% CI 0.46-0.66) and statin use (OR 0.51, 95% CI 0.40-0.64) were significantly associated with decreased 90-day mortality in subjects hospitalized with a COPD exacerbation
Paulin et al. [79] (2017)	4331	Retrospective	ARBs use seems to be associated with a lower mortality in COPD. The survival in the ARBs exposed group was 76% (CI 95% 0,69-0,81) and 71% (CI 95% 69–73%) in the non exposed group. The unadjusted HR for mortality was 0.85 (CI 95% 0.67-1.07, p = 0.17) and the adjusted HR by propensity score was 0.63 (CI 95% 0.50-0.80, p < 0.001)
Petersen et al. [80] (2014)	1170	Observational	Among ever smokers without a baseline spirometric abnormality, rapid decline was associated with an increased risk for incident COPD (OR 1.88; p = 0.003). The use of ACEi at baseline examination was protective against rapid decline, particularly among those with comorbid cardiovascular disease, hypertension, or diabetes (OR 0.48, 0.48, and 0.12, respectively; p ≤0.02 for all analyses)
Ho et al. [81] (2014)	4204	Population-based cohort	COPD patients hospitalized for first-ever COPD exacerbation receiving ARB for a cardiovascular disease, had lower in-hospital mortality (OR: 0.61; 95% CI: 0.38-0.98)
Di Marco et al. [82] (2010)	21	Double-blind, cross-over study	Enalapril did not affect the ventilatory response to exercise in COPD patients, but improved work rate and O_2 pulse
Curtis et al. [83] (2016)	80	Double-blind, placebo-controlled, parallel-group randomized controlled trial	Enalapril, together with a program of pulmonary rehabilitation, in patients without an established indication for ACEi, reduced the peak work rate response to exercise training
Zeng et al. [85] (2013)	220	Retrospective	ACEi and ARBs reduce mortality in elderly male COPD patients
Kim et al. [86] (2016)	375	Case-control	ACEi/ARBs reduce the risk of pneumonia in COPD patients (OR = 0.51, 95% CI 0.27-0.98, p = 0.04)
Parikh et al. [87] (2017)	4472	Population-based	RAS blockers are associated with slowed progression of percent emphysema on chest CT (p = 0.03)
Ekstrom et al. [88] (2013)	2249	Prospective	COPD patients receiving RAS blockers showed trends towards decreased mortality (HR, 0.90; 95% CI, 0.79-1.04; P = 0.166)
Kanazawa et al. [89] (2003)	36	Randomized double blind controlled trial	Captopril reduces mPAP in ID/II carriers
Bertoli et al. [90] (1986)	9		Captopril reduces mPAP(p < 0.05), mean pulmonary wedge pressure (p < 0.05) and total pulmonary resistance in COPD patients with pulmonary hypertension

Vasileiadis, JOURNAL OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE 2018,

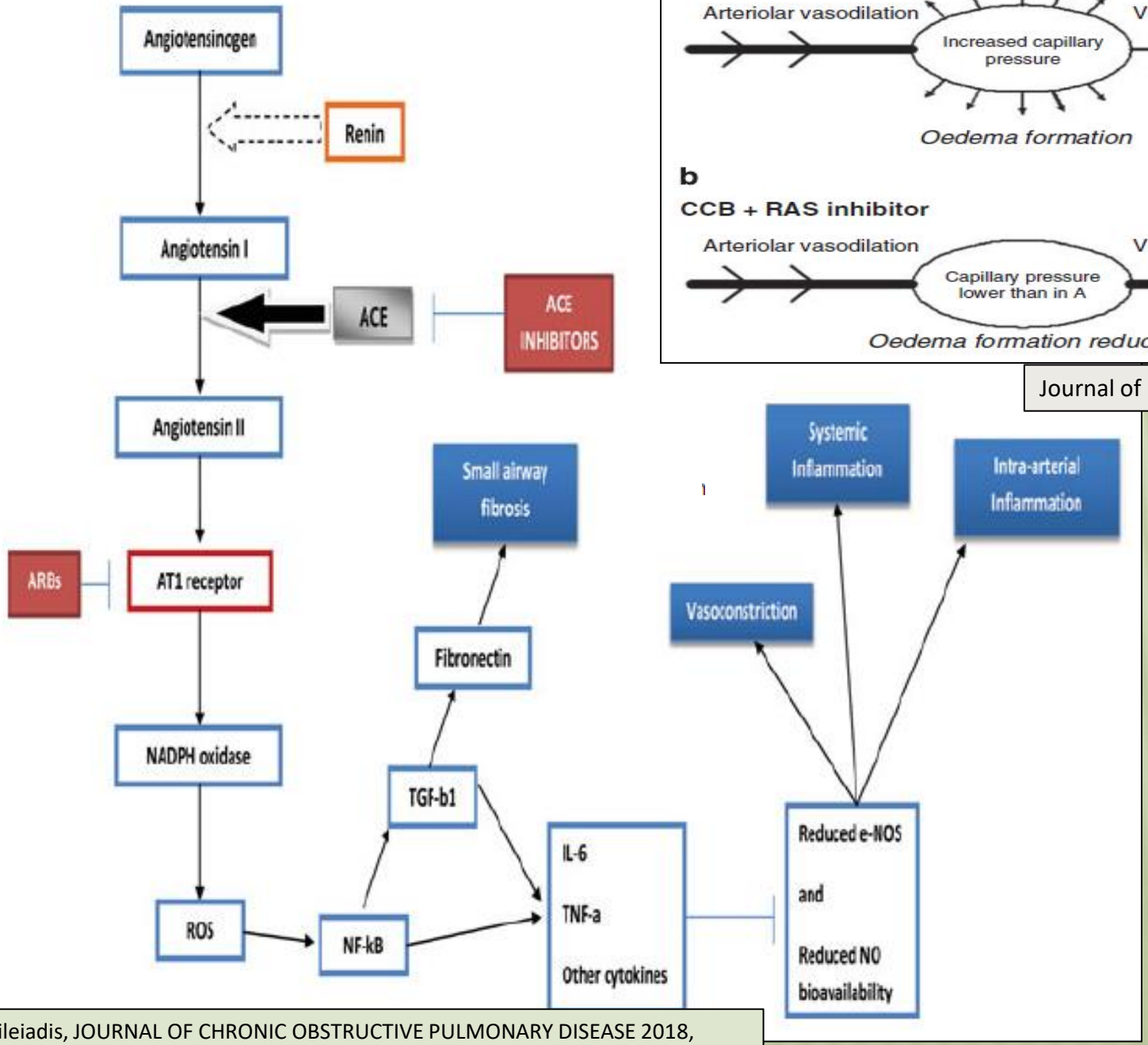
Treatment strategies in diabetes

Recommendations and statements	CoR	LoE
BP should be monitored to detect hypertension in all patients with diabetes, because it is a frequent comorbidity associated with an increase CV risk and risk for kidney events.	I	A
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 and the primary aim is to lower BP below <130/80 mmHg.	I	A
SGLT2is are recommended to reduce cardiac and kidney events in type 2 diabetes.	I	A
The non-steroidal MRA finerenone can be used, because of its nephroprotective and cardioprotective properties in patients with diabetic CKD and moderate to severe albuminuria.	I	A
There are only limited data on the potential benefits of combining SGLT2is and finerenone.	II	C

[1315]. Treatment should include a RAS blocker, because outcome-based RCTs indicate that RAS blockers prevent appearance and progression of kidney complications of diabetes more effectively than other major antihypertensive drugs, as measured by the reduced incidence of new-onset microalbuminuria, the reduction of protein excretion in proteinuric patients, the attenuated decline of GFR in diabetic and nondiabetic nephropathy and the prevention of ESKD



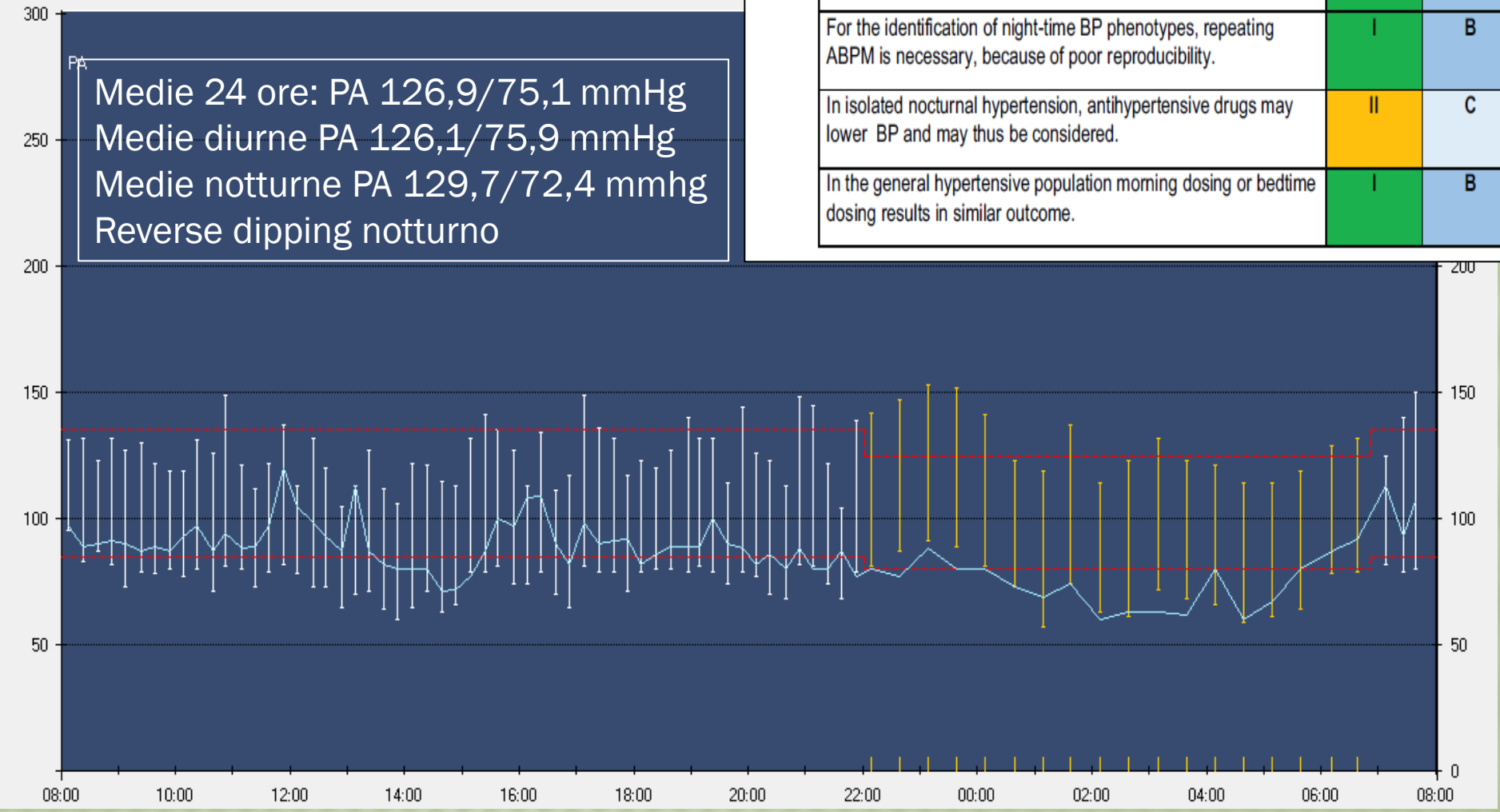
Journal of Human Hypertension (2009)



Vasileiadis, JOURNAL OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE 2018,

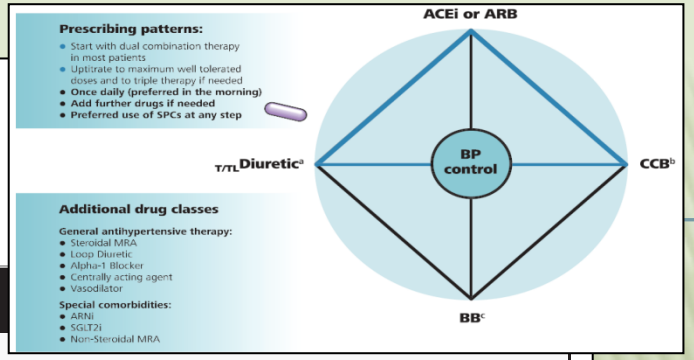
ABPM 2 (11/2023)

Medie 24 ore: PA 126,9/75,1 mmHg
Medie diurne PA 126,1/75,9 mmHg
Medie notturne PA 129,7/72,4 mmhg
Reverse dipping notturno



Night-time hypertension and BP phenotypes

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
In isolated nocturnal hypertension, antihypertensive drugs may lower BP and may thus be considered.	II	C
In the general hypertensive population morning dosing or bedtime dosing results in similar outcome.	I	B



Obstructive sleep apnea syndrome and hypertension
K Kario

Obstructive sleep apnea

Negative intrathoracic pressure ↑

Pulmonary stretch receptor stimulation ↓

Chemoreceptor stimulation ↑

Microarousal

Hypoxia (periodic)

Hypercapnea (periodic)

Sympathetic nerve activity ↑

Baroreceptor sensitivity ↓

RAA system ↑

Endothelin ↑

Insulin resistance ↑

Oxidative stress ↑

Inflammation ↑

Endothelial dysfunction

Nitric oxide ↓

Hypertension

Non-dipper / Riser pattern

Hypertensive targert organ damage

Hypertensive heart disease

LV hypertrophy
Diastolic function
Left atrial enlargement

Silent cerebral disease

Silent cerebral infarcts
White matter disease

Microalbuminuria

Kario, Hypertension Researche 2009

TABLE 16. Selected diseases and conditions for the use of BBs in patients with hypertension [591]

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 rec
Glaucoma
Thyrotoxicosis, hyperthyroidism
Hyperparathyroidism in uremia
Migraine headache
Essential tremor
Performance anxiety and anxiety disorders
Psychiatric disorders (posttraumatic stress)

Recommendations and statements	CoR	LoE
In adults with elevated BP who are overweight or obese, weight reduction is recommended to reduce BP and improve CV outcomes.	I	A
Thiazide/Thiazide-like Diuretics and BBs have some unfavorable metabolic effects. However, since optimal BP control is the primary goal of antihypertensive treatment, combination therapy with these drug classes is frequently necessary and recommended.	I	A

2023 ESH Guidelines

Title

Association of β-Blocker Use with Survival and Pulmonary Function in Patients with COPD and CVD

Summary

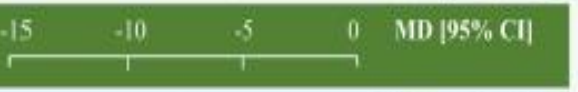
To clarify the effect of BBs on respiratory function and survival in COPD patients with CVD as well as the difference between the effects of cardioselective and noncardioselective BBs.

Data sources

Results

Outcome	Samples	Number of Studies included	Comparison	Patients	HR [95% CI]
COPD exacerbation	183685	17	BB vs no BB	COPD+CVD	0.77 [0.67, 0.89]
	17834	7	selective BB vs no BB	COPD+CVD	0.72 [0.56, 0.94]
	17455	5	nonselective BB vs no BB	COPD+CVD	0.98 [0.71, 1.34]
	41183	4	selective BB vs nonselective B	COPD+CVD	1.00 [0.91, 1.10]
	20252	4	BB vs no BB	COPD+CHF	0.83 [0.56, 1.23]
Hospital mortality	108459	5	BB vs no BB	COPD+CVD	0.67 [0.46, 0.99]
All-cause mortality	335419	22	BB vs no BB	COPD+CVD	0.69 [0.58, 0.81]
	44775	8	selective BB vs no BB	COPD+CVD	0.60 [0.48, 0.76]
	17624	4	nonselective BB vs no BB	COPD+CVD	0.72 [0.58, 0.91]
	30691	6	BB vs no BB	COPD+CHF	0.62 [0.53, 0.74]
	33067	4	BB vs no BB	COPD+MI	0.87 [0.82, 0.91]

Outcome	Samples	Number of Studies included	Comparison	Patients	MD [95% CI]
Heart rate	5473	5	BB vs no BB	COPD+CVD	-7.87 [-11.12, -4.62]



Yang, European Heart Journal (2020)

Supplementary table 1. Conclusions on extrapulmonary manifestations of COPD and comorbidities

	Conclusions (C) and Recommendations (R)	Final results	Level of evidence (LE)/Grade of recommendation (GR)	Source
Comorbidities				
B) ARTERIAL HYPERTENSION (AHT)				
Consequences of AHT in COPD				
7.	A comprehensive evaluation must be performed to detect risk factors associated with COPD and AHT in all patients with both diseases, since these conditions will foster the development of cardiovascular diseases, such as ischemic heart disease and congestive heart failure, that worsen the prognosis of COPD patients.	Consensus (95.7%) 1st round	5 D	Adapted from [10] Reference: [13]
Treatment of patients with COPD and AHT				
7.	Bronchodilators (long acting muscarinic antagonists and long acting beta agonists) are safe and well tolerated in hypertensive patients with COPD.	Unanimity 1st round	5	Reference: [14]
7.	Treatment of AHT is the same in patients with and without COPD, and COPD treatment is the same in patients with and without AHT.	Unanimity 1st round	5	Expert opinion
7.	The use of beta-blockers, especially cardioselective agents, is recommended in hypertensive patients with COPD and ischemic heart disease or heart failure.	Unanimity 1st round	2 B	Adapted from [15] References: [16,17]
7.	Cardioselective beta-blockers should not be suspended during acute COPD exacerbations.	Consensus (91.3%) 1st round	2 B	Compiled by authors Reference: [18]
7.	In patients with COPD and AHT, antihypertensive treatment with angiotensin converting enzyme inhibitors and angiotensin receptor II blockerss is recommended.	Consensus (91.3%) 1st round	5 D	Adapted from [10] Expert opinion
7.	COPD should be treated according to standard clinical practice guideline recommendations, since there is no direct evidence that COPD should be treated differently in the presence of hypertension.	Unanimity 1st round	5 D	Compiled by authors Expert opinion

Role of α1-blockers in the current management of hypertension

Hua Li MD[1] | Ting-Yan Xu MD, PhD[1] | Yan Li MD, PhD[1]

TABLE 1 Role of α1-blockers in the current management of hypertension

Indication	Epidemiology	Mechanism of action	Treatment effect
Benign prostatic hypertrophy	Up to 25% of hypertensive patients older than 60 years of age	Inhibition of prostatic smooth muscle tone and relaxation of the prostate	Blood pressure lowering and alleviation of lower urinary tract symptoms
Resistant hypertension	13.7% treated hypertension[34]	Add-on therapy	Blood pressure lowering and control
Primary aldosteronism screen	6%–8% in primary care[39,40]; 15% in resistant hypertension[41]	No or little effect on plasma aldosterone-to-renin ratio	Blood pressure control

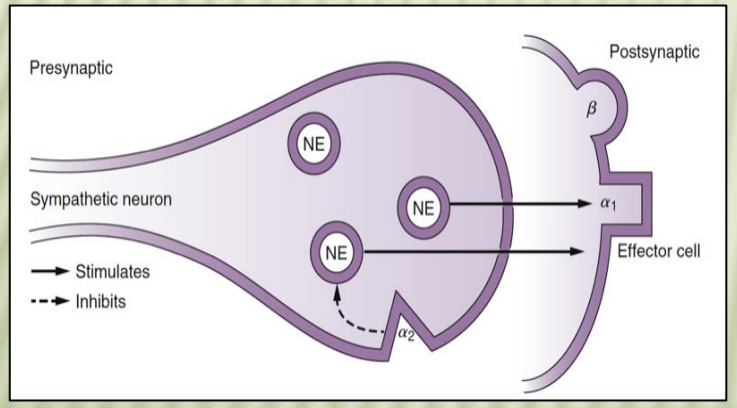


TABLE 2 Key points in the use of α1-blockers in the current management of hypertension

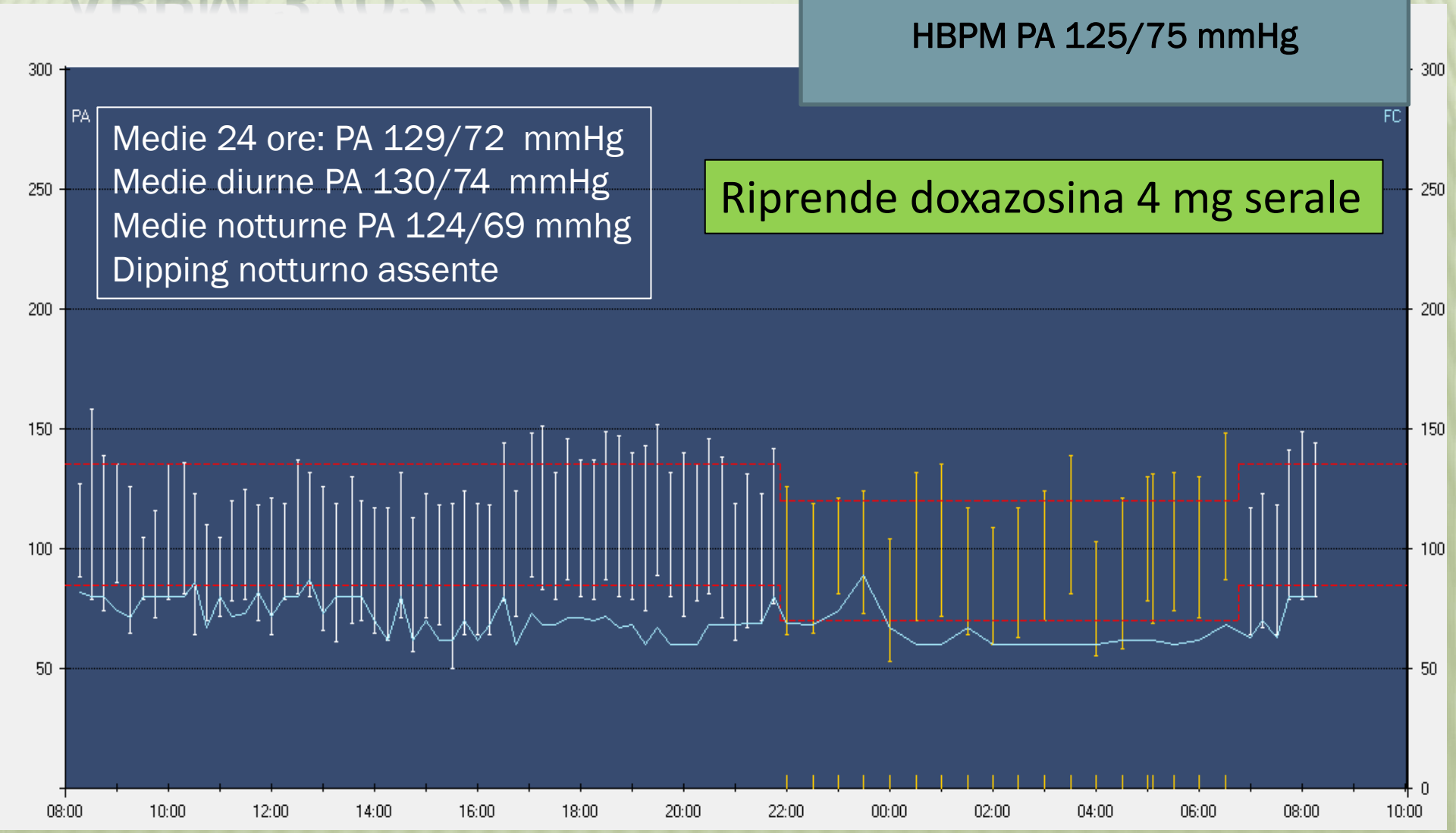
Key point	Therapeutic suggestion
Choice of agents	Long acting agents, for example, doxazosin gastrointestinal therapeutic system or terazosin
Prevention of orthostatic hypotension	Careful initial dosing and no overdosing
Fluid retention	Combination with a diuretic
Intraoperative Floppy Iris Syndrome[57]	Patients should be educated with regard to this possible side effect particularly when cataract surgery is considered

Hua Li, *J Clin Hypertens*. 2022

ABPM 3 (02/2024)

PA OFFICE:
128/80 mmHg
In ortostasi PA 120/85 mmHg

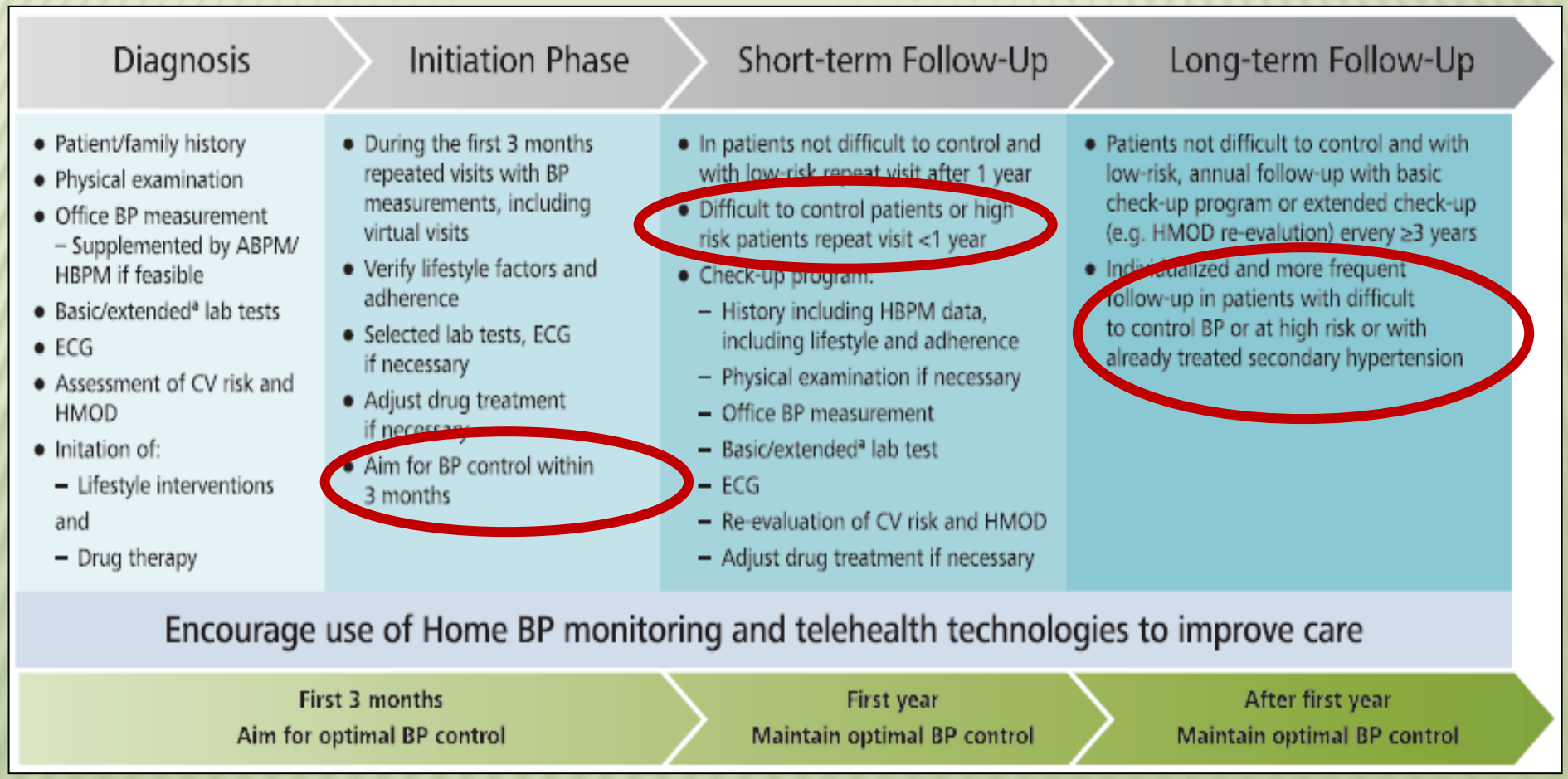
HBPM PA 125/75 mmHg



Medie 24 ore: PA 129/72 mmHg
Medie diurne PA 130/74 mmHg
Medie notturne PA 124/69 mmhg
Dipping notturno assente

Riprende doxazosina 4 mg serale

FOLLOW-UP OF PATIENTS WITH HYPERTENSION



2023 ESH Guidelines

CONCLUSIONI

- Inadeguato controllo pressorio per: sottoutilizzo delle terapie combinate, combinazioni irrazionali, inerzia terapeutica dei medici e scarsa aderenza al trattamento
- Aderenza e persistenza sono necessarie all'efficacia della terapia antipertensiva
- Scarse aderenza e persistenza sono causa di HMOD, peggiori outcomes ed incremento dei costi sanitari
- Indagare su eventuale ridotta aderenza e sui suoi motivi, prima ancora di sospettare ipertensione resistente o forme secondarie
- Considerare la terapia di combinazione tra più farmaci nella maggior parte dei pazienti, a meno di valori pressori < 150 mmHg, o pazienti fragili o anziani.
- La SPC aumenta l'aderenza terapeutica e l'ottenimento dei target pressori
- Ipertensione di difficile controllo non coincide con ipertensione resistente
- E' più corretto spostare l'attenzione sul paziente «difficile da trattare»


Grazie per l'attenzione