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BP Goals: Updates and Practical Approaches to Hypertension Guideline Implementation

*A Glance at ACC/AHA and LASH Guidelines:
Highlights and Potential Gaps in Hypertension*

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Disclosure of Potential Conflicts of Interest (David Brasil)

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Sponsored in transport and/or hotel accommodations in Congresses/Conferences	Servier
Sponsored in clinical trials and/or in basic research funded by pharmaceutical companies	Bayer - National Lead Investigator Voyager-PAD Clinical Trial
Speaker in meetings sponsored by pharmaceutical companies	Servier, LIBBS
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Receive institutional support from pharmaceutical companies	—
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Hypertension Guidelines that Impact Clinical Practice in Brazil and Latin America



7TH BRAZILIAN GUIDELINE OF ARTERIAL HYPERTENSION

Volume 107, Nº 3, September 2016

Indexing: ISI (Thomson Scientific), Cumulated Index Medicus (NLM), SCOPUS, MEDLINE, EMBASE, LILACS, SciELO, PubMed **September 2016**

Guidelines on the management of arterial hypertension and related comorbidities in Latin America

Journal of Hypertension 2017, 35:000–000

LASH - April 2017

Task Force of the Latin American Society of Hypertension*

Whelton PK, et al.

2017 High Blood Pressure Clinical Practice Guideline

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



ESC
European Society
of Cardiology

European Heart Journal (2018) 00, 1–98
doi:10.1093/eurheartj/ehy339

ESC/ESH GUIDELINES

2018 ESC/ESH Guidelines for the management of arterial hypertension
August 2018



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

Categories of BP in Adults*

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

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

Table 6

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Guidelines on the management of arterial hypertension and related comorbidities in Latin America

Task Force of the Latin American Society of Hypertension

Blood Pressure Classification According to LASH

Classification	SBP (mmHg)	DBP (mmHg)
Normotension		
Optimal BP	<120	<80
Normal BP	120–129	80–84
High-normal BP	130–139	85–89
Hypertension		
Grade 1	140–159	90–99
Grade 2	160–179	100–109
Grade 3	≥180	≥110
Isolated systolic hypertension	≥140	<90

When SBP and DBP values are in different BP categories, the individual should be classified in the higher BP category. BP, blood pressure.

Task Force of the Latin American Society of Hypertension.
***J Hypertens* 2017;35(8):1529-45.**



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BP Goal for Patients With Hypertension

Recommendations for BP Goal for Patients With Hypertension

References that support recommendations are summarized in Online Data Supplement 26 and Systematic Review Report.

COR	LOE	Recommendations
I	SBP: B-R ^{SR}	1. For adults with confirmed hypertension and known CVD or 10-year ASCVD event risk of 10% or higher (see Section 8.1.2), a BP target of less than 130/80 mm Hg is recommended (1-5).
	DBP: C-EO	
IIb	SBP: B-NR	2. For adults with confirmed hypertension, without additional markers of increased CVD risk, a BP target of less than 130/80 mm Hg may be reasonable (6-9).
	DBP: C-EO	

SR indicates systematic review.

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Guidelines on the management of arterial hypertension and related comorbidities in Latin America

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Antihypertensive Pharmacologic Treatment Based on 5 Major Classes of Drugs

- ✓ **Diuretics (*i.e.*, chlorthalidone, indapamide or thiazides)**
- ✓ **Calcium Channel Blockers (CCB)**
- ✓ **Angiotensin-Converting-Enzyme Inhibitors (ACE-I)**
- ✓ **Angiotensin Receptor Blockers (ARB)**
- ✓ **Beta-blockers**

(all drug classes above are suitable for initiation and maintenance of antihypertensive treatment alone or in combination)

PREFER ANTI-HYPERTENSIVE AGENTS WITH:

- o 24 hour BP control (once daily dose)
- o Proven reduction of cardiovascular event risk
- o Low cost (especially in low-income people)

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J Hypertens 2017;35(8):1529-45.



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Oral Antihypertensive Drugs (1 of 3)

Class	Drug	Usual Dose, Range (mg per day)*	Daily Frequency	Comments
Primary Agents				
Thiazide or thiazide-type diuretics	Chlorthalidone	12.5–25	1	<ul style="list-style-type: none"> Chlorthalidone preferred based on prolonged half-life and proven trial reduction of CVD Monitor for hyponatremia and hypokalemia, uric acid and calcium levels. Use with caution in patients with history of acute gout unless patient is on uric acid-lowering therapy.
	Hydrochlorothiazide	25–50	1	
	Indapamide	1.25–2.5	1	
	Metolazone	2.5–10	1	
ACE Inhibitors	Benazepril	10–40	1 or 2	<ul style="list-style-type: none"> Do not use in combination with ARBs or direct renin inhibitor Increased risk of hyperkalemia, especially in patients with CKD or in those on K⁺ supplements or K⁺-sparing drugs May cause acute renal failure in patients with severe bilateral renal artery stenosis Do not use if history of angioedema with ACE inhibitors. Avoid in pregnancy
	Captopril	12.5–150	2 or 3	
	Enalapril	5–40	1 or 2	
	Fosinopril	10–40	1	
	Lisinopril	10–40	1	
	Moexipril	7.5–30	1 or 2	
	Perindopril	4–16	1	
	Quinapril	10–80	1 or 2	
	Ramipril	2.5–10	1 or 2	
ARBs	Trandolapril	1–4	1	
	Azilsartan	40–80	1	<ul style="list-style-type: none"> Do not use in combination with ACE inhibitors or direct renin inhibitor Increased risk of hyperkalemia in CKD or in those on K⁺ supplements or K⁺-sparing drugs May cause acute renal failure in patients with severe bilateral renal artery stenosis Do not use if history of angioedema with ARBs. Patients with a history of angioedema with an ACEI can receive an ARB beginning 6 weeks after ACEI discontinued. Avoid in pregnancy
	Candesartan	8–32	1	
	Eprosartan	600–800	1 or 2	
	Irbesartan	150–300	1	
	Losartan	50–100	1 or 2	
	Olmesartan	20–40	1	
	Telmisartan	20–80	1	
	Valsartan	80–320	1	
CCB—dihydropyridines	Amlodipine	2.5–10	1	<ul style="list-style-type: none"> Avoid use in patients with HFrEF; amlodipine or felodipine may be used if required Associated with dose-related pedal edema, which is more common in women than men
	Felodipine	5–10	1	
	Isradipine	5–10	2	
	Nicardipine SR	5–20	1	
	Nifedipine LA	60–120	1	
	Nisoldipine	30–90	1	
CCB—nondihydropyridines	Diltiazem SR	180–360	2	<ul style="list-style-type: none"> Avoid routine use with beta blockers due to increased risk of bradycardia and heart block Do not use in patients with HFrEF Drug interactions with diltiazem and verapamil (CYP3A4 major substrate and moderate inhibitor)
	Diltiazem ER	120–480	1	
	Verapamil IR	40–80	3	
	Verapamil SR	120–480	1 or 2	
	Verapamil-delayed onset ER (various forms)	100–480	1 (in the evening)	

Table is continued in the next two pages

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

Primary Antihypertensive Agents

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Initiation and Maintenance of Antihypertensive Drug Therapy:

Monotherapy versus Combination

GRADE 1

WITH LOW CV RISK

Initiate with MONOTHERAPY:

- I. DIURETICS (Thiazides, Chlorthalidone, Indapamide)
- II. ACEIs
- III. ARBs
- IV. CCBs
- V. BETA-BLOCKERS

➤ FIXED DOSE COMBINATION:
MAY ALSO BE PRESCRIBED AS 1ST LINE

WITH MODERATE or HIGH CV RISK

Prefer FIXED DOSE COMBINATION:

- I. ACEI or ARB + CCB or DIURETIC
- II. See text for special conditions

GRADE 2

WITH ANY LEVEL of CV RISK

Prefer FIXED DOSE COMBINATION:

- I. ACEI or ARB + CCB or DIURETIC
- II. If necessary ACEI/ARB, and DIURETIC
- III. See text for special conditions

Task Force of the Latin American Society of Hypertension.
J Hypertens 2017;35(8):1529-45.



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Choice of Initial Monotherapy Versus Initial Combination Drug Therapy

Recommendations for Choice of Initial Monotherapy Versus Initial Combination Drug Therapy*		
COR	LOE	Recommendation
I	C-EO	1. Initiation of antihypertensive drug therapy with 2 first-line agents of different classes, either as separate agents or in a fixed-dose combination, is recommended in adults with stage 2 hypertension and an average BP more than 20/10 mm Hg above their BP target.
Ila	C-EO	2. Initiation of antihypertensive drug therapy with a single antihypertensive drug is reasonable in adults with stage 1 hypertension and BP goal <130/80 mm Hg with dosage titration and sequential addition of other agents to achieve the BP target.

*Fixed-dose combination antihypertensive medications are listed in Online Data Supplement D.

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Specific Conditions & Comorbidities in Which Certain Antihypertensive Drug Classes May Be Preferable a First Choice

- (1) ACE-Is or ARBs in patients with metabolic syndrome or type 2 diabetes; because metabolic variables are not affected or may even be improved by these agents,
- (2) ACE-Is or ARBs in patients with renal dysfunction and microalbuminuria or proteinuria, because these agents slow progression to chronic renal failure and dialysis,
- (3) ACE-Is or ARBs in patients with systolic or diastolic LV dysfunction,
- (4) ACE-Is, ARBs and CCBs in patients with LV hypertrophy, because these agents facilitate LV hypertrophy regression,
- (5) β -blockers in patients with coronary heart disease,
- (6) CCBs (dihydropyridines) or diuretics in elderly hypertensive patients with isolated systolic hypertension and in hypertensive patients of African descent,
- (7) Alpha blocking agents, in patients with prostatic hypertrophy,
- (8) Chlorthalidone, indapamide or thiazides in African Americans, elderly hypertensive patients or low-income people, who cannot afford the cost of other drugs,



- (9) Diuretics, ACE-Is, β -blockers (metoprolol, bisoprolol, carvedilol or nebivolol) and aldosterone antagonists, in hypertensive patients with heart failure,

- (10) ACE-Is and β -blockers, in post MI patients,



- (11) Diuretics (slow release indapamide) possibly associated with an ACE-I in the prevention of recurrent stroke,

- (12) Patients with peripheral vascular disease (in addition to smoking cessation and regular aerobic exercise) may be prescribed CCBs to lower BP without exacerbation of symptoms,



- (13) ACE-Is or ARBs, in patients with recurrent atrial fibrillation; β -blockers or verapamil in sustained atrial fibrillation

- (14) Mineralocorticoid receptor antagonists, mainly spironolactone and/or an alpha blocker, in resistant hypertension.

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Guideline for the Prevention, Detection, Evaluation, and Management
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BP threshold for patients over 65yo

10.3.1. Older Persons

Recommendations for Treatment of Hypertension in Older Persons		
References that support recommendations are summarized in Online Data Supplement 54.		
COR	LOE	Recommendations
I	A	1. Treatment of hypertension with a SBP treatment goal of less than 130 mm Hg is recommended for noninstitutionalized ambulatory community-dwelling adults (≥65 years of age) with an average SBP of 130 mm Hg or higher (1).
Ila	C-EO	2. For older adults (≥65 years of age) with hypertension and a high burden of comorbidity and limited life expectancy, clinical judgment, patient preference, and a team-based approach to assess risk/benefit is reasonable for decisions regarding intensity of BP lowering and choice of antihypertensive drugs.

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Hypertension in Elderly

- However, it is the Task Force opinion that the very favorable results of all these trials make it prudent to initiate antihypertensive therapy also in elderly grade 1 hypertensive patients provided they are in good physical conditions and do not present important adverse reactions to treatment, such as excessive or orthostatic hypotension, dizziness and physical or mental deterioration.
- CCBs (dihydropyridines) or diuretics in elderly hypertensive patients with isolated systolic hypertension and in hypertensive patients of African descent,
- Chlorthalidone, indapamide or thiazides in African Americans, elderly hypertensive patients or low-income people, who cannot afford the cost of other drugs,

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J Hypertens 2017;35(8):1529-45.



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Guideline for the Prevention, Detection, Evaluation, and Management
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BP Thresholds for and BP Goals of Pharmacologic Therapy in Patients with Hypertension According to Clinical Conditions

***J Am Coll Cardiol* 2018;71(19):2199-2269**

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

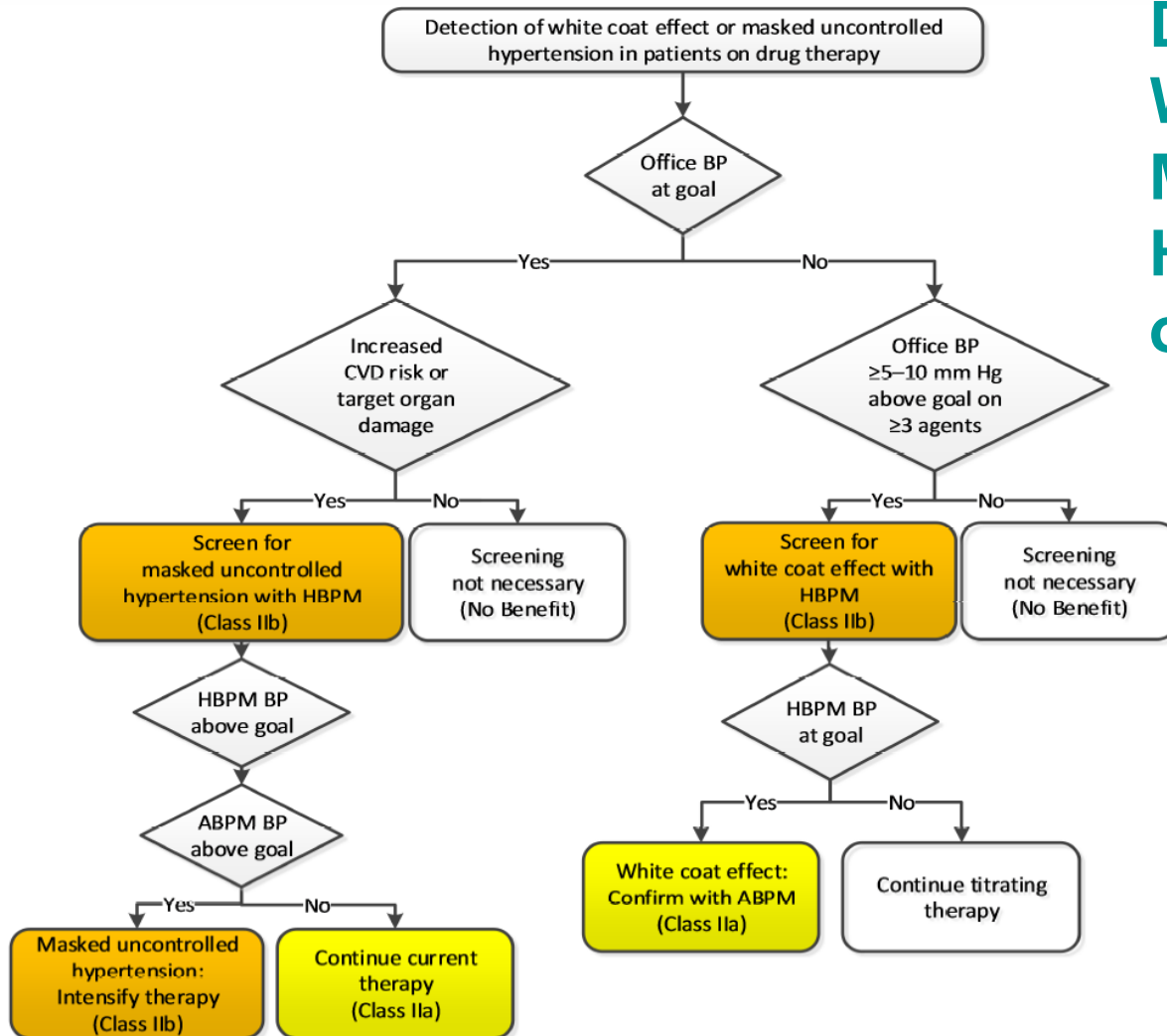


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Detection of White Coat Effect or Masked Uncontrolled Hypertension in Patients on Drug Therapy



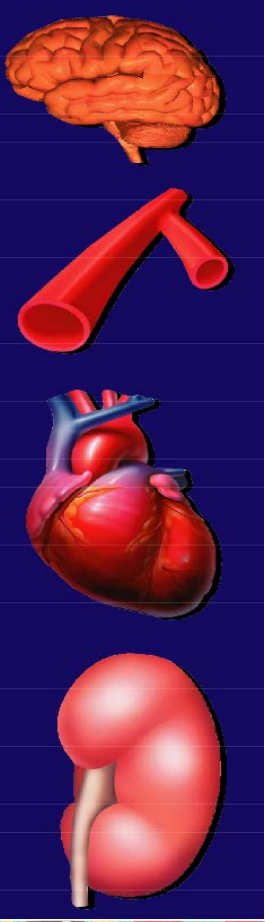
J Am Coll Cardiol 2018;71(19):2199-2269.



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Masked uncontrolled hypertension

MUCH:

- Out-of-office BP measurements fundamental to interpret
- Mostly Registry-based information

- Occurs in 30% of treated hypertensive patients
- More common with comorbidities such as DM and CKD, and in high risk patients
- More commonly due to poorly controlled nocturnal rather than daytime pressures on ABPM
- Presently, no data are available from outcome trials for patients with MUCH

Eur Heart J 2018;39(33):3021-3104



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The ACC/AHA Guidelines document provides ABPM equivalent values...

Table 11. Corresponding Values of SBP/DBP for Clinic, HBPM, Daytime, Nighttime, and 24-Hour ABPM Measurements

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Clinic	HBPM	Daytime ABPM	Nighttime ABPM	24-Hour ABPM
120/80	120/80	120/80	100/65	115/75
130/80	130/80	130/80	110/65	125/75
140/90	135/85	135/85	120/70	130/80
160/100	145/90	145/90	140/85	145/90

ABPM indicates ambulatory blood pressure monitoring; BP, blood pressure; DBP diastolic blood pressure; HBPM, home blood pressure monitoring; and SBP, systolic blood pressure.

The LASH Guidelines definition of HTN by different types of BP measurements...

	SBP (mmHg)		DBP (mmHg)
Office BP	≥ 140	Or	≥ 90
Home BP	≥ 135	Or	≥ 85
Ambulatory BP			
Daytime	≥ 135	Or	≥ 85
Night-time	≥ 120	Or	≥ 70
24 h	≥ 130	Or	≥ 80

BP, blood pressure.

Yes, indeed...

But... What are the optimal BP treatment targets according to HBPM and ABPM?



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Gaps in
Hypertension

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA
Guideline for the Prevention, Detection, Evaluation, and Management
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Role and Comprehensiveness of ABPM and HBPM in Hypertension Management: (ABPM and HBPM provide enhanced ability to both diagnose hypertension and monitor treatment)

Gaps in
Hypertension

- Relationship of outcomes to ABPM and HBPM measurements (?)
- Can we develop definitions of HTN severity based on these measures (?)
- Based on ABPM /HBPM measures, can we score the importance of:
 - Masked HTN (?)
 - White Coat HTN (?)
 - Nocturnal HTN (?)
- Reproducibility of ABPM across a broader range of ethnicities (?)
- Practicable incorporation of ABPM into EHR and routine HTN care (?)



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Left Ventricular Hypertrophy and Heart Failure

J Am Coll Cardiol 2018;71(19):2199-2269.

Heart Failure with Reduced Ejection Fraction (HFrEF)

Recommendations for Treatment of Hypertension in Patients with Heart Failure with Reduced Ejection Fraction (HFrEF) Referenced studies that support recommendations are summarized in online Data Supplement 34		
COR	LOE	Recommendations
I	C-EO	1. Adults with HFrEF and hypertension should be prescribed GDMT* titrated to attain a BP less than 130/80 mm Hg.
III: No Benefit	B-R	2. Nondihydropyridine CCBs are not recommended in the treatment of hypertension in adults with HFrEF.

Heart Failure with Preserved Ejection Fraction (HFpEF)

Recommendations for Treatment of Hypertension in Patients with Heart Failure with Preserved Ejection Fraction (HFpEF) Referenced studies that support recommendations are summarized in online Data Supplement 35, 36		
COR	LOE	Recommendations
I	C-EO	1. In adults with HFpEF who present with symptoms of volume overload, diuretics should be prescribed to control hypertension.
I	C-LD	2. Adults with HFpEF and persistent hypertension after management of volume overload should be prescribed ACE inhibitors or ARB and beta blockers titrated to attain systolic BP less than 130 mm Hg.

TABLE 3. Echocardiogram measurements for left ventricular hypertrophy and diastolic dysfunction

Measurements	Abnormal
Left ventricular mass index (g/m ²)	>95 (women), >115 (men)
Relative wall thickness	>0.42
Septal velocity (e') (cm/s)	<8
Lateral wall velocity (e') (cm/s)	<10
Left atrial volume (ml/m ²)	≥34
Left ventricular filling pressure (e/e')	≥13

Task Force of the Latin American Society of Hypertension.
J Hypertens 2017;35(8):1529-45.



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Left Ventricular Hypertrophy

Remaining Questions - Gaps in Guidelines



Gaps in Hypertension

- Should all patients with hypertension be screened with TTEcho for LVH? If NOT, what patient's profile should be an evidence-based recommendation for LVH screening on a daily practice (?)
- Should TTEcho/MRI be repeated once LVH is noted (?)
- Is it important to document LVH regression as for prevention of future HFpEF (?)



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Additional Gaps in Current Existing Hypertension Guidelines

➤ What is the incremental benefit for CV risk prediction when the ASCVD risk is less than 10% (?)

- HTN is undertreated in women. Nevertheless, there is no widespread education to practitioners about this fact and very few data in women
- Limited recommendation on BP during pregnancy

➤ Optimal treatment in different ethnic groups (?)

➤ Optimal treatment in young patients (< 40 yo) (?)

➤ Optimal treatment targets in specific clinical conditions
e.g. diabetes, CKD, and post-stroke (?)

“The value of experience is not in seeing much, but in seeing wisely.” Sir William Osler



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