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Review Article

Medical Management of Hypertensive Heart Failure

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Abstract

Hypertension is an important risk factor of heart failure (HF). HF is a common cardiovascular disease, which carries a poor prognosis. Antecedent hypertension is present in 3/4th of chronic HF patients. The risk of HF increases by 50% with 20 mmHg elevation of systolic blood pressure (BP). Among patients with HF, those with higher levels of systolic and diastolic BP are at greater risk of adverse events. Thus, optimal treatment of hypertension is vital in reducing the risk of incident HF and HF hospitalization.

Key words: Hypertension, heart failure with preserved ejection fraction (HFpEF), heart failure with reduced ejection fraction (HFrEF)

Introduction

Hypertension is an important risk factor of cardiovascular disease (CVD), including heart failure (HF);[1] antecedent hypertension is present in 75% of patients with chronic HF.[2] On the other hand, people with normal blood pressure (BP) at middle age have lower risk of developing HF during the remaining course of life.[3]

HF is a common disease. It carries a poor prognosis, which rivals that of cancer. The 5-year survival rate is 25% in men and 38% in women.[4] The risk of HF increases with age. The annual incidence of HF in men is 3/1000 from 50 to 59 years of age and 27/1000 from 80 to 89 years, whereas in women it is 2/1000 and 22/1000, respectively.[4]

HF is among the most common consequences of hypertensive heart disease (HHD), along with ischemic heart disease and arrhythmias.[5] In the Framingham Heart Study, the risk of HF increased by 50% with 20 mmHg elevation of systolic BP.[6,7]

Hypertension and myocardial infarction (MI) are the two most important risk factors for developing HF.[8-10]

MI confers the greatest risk of developing HF. However, due to its high prevalence, hypertension carries the greatest population-attributable risk, accounting for 39% of cases in men and 59% in women.[11] Among patients with HF, those with higher levels of systolic and diastolic BP are at greater risk of adverse events.[12] Thus, optimal treatment of hypertension is vital in reducing the risk of incident HF and HF hospitalization.[13-15]

Definition

HF is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling (diastolic) or ejection of blood (systolic). The cardinal manifestations of HF are dyspnea and fatigue, which may limit exercise tolerance, and fluid retention, which may lead to pulmonary and/or splanchnic congestion and/or peripheral edema.

The ESC 2016 guidelines classify HF into three types based on the left ventricular ejection fraction (LVEF) [Table 1]. HF with LVEF ≥50% is defined as HF with preserved EF (or diastolic HF). HF with LVEF <40% is defined as HF with reduced EF (or systolic HF). HF with LVEF in the range of 40–49% is defined as HF with mid-range EF (HFmrEF). Patients with HFmrEF have mild systolic dysfunction, along with features of diastolic dysfunction.[16]

Pathophysiology

Long-standing systemic arterial hypertension results in sustained cardiac pressure overload. This results in structural and functional changes in the left ventricular (LV) myocardium as an adaptive response, known as cardiac remodeling. LV diastolic dysfunction is the first abnormal cardiac feature in most cases of hypertension. The other common finding in pressure overload is concentric LV hypertrophy (increase in LV mass at the expense

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of LV volume).[3] On the other hand, in cases of predominant volume overload, cardiac remodeling consists of eccentric hypertrophy (increase in LV mass and volume).[17]

In case of sustained pressure overload, there is progression of diastolic dysfunction of the concentric hypertrophied LV, which results in HF with preserved ejection fraction (HFpEF). Further progression of HFpEF results in LV systolic insufficiency (HF with reduced ejection fraction [HFrEF]), a so-called "burn-out" of LV. Whereas, in case of sustained volume overload, there is progression of LV dilatation, followed by decompensation of the eccentric hypertrophied LV, which results in HFrEF.[3,18]

Based on the pathophysiologic and clinical features, HHD is classified into four categories:

- Degree I: Isolated LV diastolic dysfunction with no LV hypertrophy
- Degree II: LV diastolic dysfunction with concentric LV hypertrophy
- Degree III: Clinical HF (dyspnea and pulmonary edema with preserved ejection fraction)
- Degree IV: Dilated cardiomyopathy with HFrEF.[19]

Based on the development and progression of disease, HF can be classified into various stages:

- Stage A – At high risk for HF but without structural heart disease or symptoms of HF
- Stage B – Structural heart disease but without signs or symptoms of HF
- Stage C – Structural heart disease with prior or current symptoms of HF
- Stage D – Refractory HF requiring specialized interventions.[20]

Investigation in Hypertensive HF

Initial investigation

Plasma natriuretic peptides (NPs)

Plasma concentration of NPs is a useful initial investigation, especially in non-acute patients when echocardiography cannot be done immediately. The other common use lies in the monitoring of HF treatment in the in-patient setting. In acute HF, the upper limit of normal value for B-type NP (BNP) is 100 pg/mL and for N-terminal pro-BNP (NT-proBNP) is 300 pg/mL. In non-acute patients, the upper limit of normal for BNP is 35 pg/mL and for NT-proBNP is 125 pg/mL. Diagnostic values are similar for both HFrEF and HFpEF, although values for HFpEF are usually lower than for HFrEF.[16]

Due to the various cardiovascular and non-cardiovascular causes of elevated NPs apart from HF, including age, atrial fibrillation, and renal failure, the use of NPs is recommended to rule out HF, but not necessarily for establishing the diagnosis.[16]

Electrocardiogram

ECG changes commonly seen in hypertensive HF patients include LV hypertrophy and left atrial enlargement. Atrial fibrillation may be present in some cases since hypertension is a known predisposing factor for AF. In some cases, ECG may provide clue regarding the etiology, like MI. On the other hand, patients with a completely normal ECG are unlikely to have HF (sensitivity 89%).[16]

Echocardiography

Echocardiography is the most useful, widely available test to aid in the diagnosis of HF. It provides important information on ventricular function, chamber volumes, wall thickness, and valve function, which is vital in the diagnosis and treatment of HF.[16]

Chest X-ray

Chest X-ray is more useful to identify an alternative, pulmonary explanation for a patient's clinical findings, rather than for diagnosing HF. In acute HF, chest X-ray shows features of pulmonary venous congestion or edema. The absence of cardiomegaly on X-ray does not exclude significant LV dysfunction.[16]

Further Investigation

HF due to uncontrolled/longstanding hypertension is a manifestation of hypertension-mediated organ damage (HMOD). The presence of extensive HMOD is one of the indications to evaluate the patient for secondary causes of hypertension. Therefore, apart from routine evaluation, the purpose of investigating these groups of patients would be to:

1. Assess the extent of HMOD
2. Look for secondary causes of hypertension.

However, the above rationale might not always be applicable for hypertensive patients who have HF due to other causes, such as MI.

Assessment of HMOD

HMOD refers to structural or functional changes in arteries or end organs (heart, blood vessels, brain, eyes, and kidney) caused by an elevated BP. The presence of HMOD is a marker of pre-clinical or asymptomatic CVD, and indicates an increased cardiovascular risk to the patient.[20,21] Early recognition and treatment of hypertension are important, which may delay the progression of HMOD and will reduce the elevated CV risk of these patients.[22] The various investigations to establish HMOD are shown in Table 2.[23]

Evaluation for Secondary Hypertension

Secondary hypertension is hypertension due to an identifiable cause, which may be treatable with an intervention specific to the cause.[24] The prevalence of secondary hypertension is 5–15% among hypertensive patients.[23]

There are certain patient characteristics that should raise the suspicion of secondary hypertension [Table 3].

HF due to uncontrolled hypertension is a manifestation of HMOD. The presence of extensive HMOD should raise suspicion to rule out secondary causes of hypertension.

The common causes of secondary hypertension and screening tests are described in Table 4.

Table 1: Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF), and reduced ejection fraction (HFrEF)[16]

Type of HF		HFrEF	HFmrEF	HFpEF
Criteria	1	Symptoms±signs	Symptoms±signs	Symptoms±signs
	2	LVEF <40%	LVEF 40-49%	LVEF ≥50%
	3	-	1. Elevated natriuretic peptide levels 2. At-least one additional criterion a. relevant structural heart disease (LVH and/or LAE) b. diastolic dysfunction	1. Elevated natriuretic peptide levels 2. At-least one additional criterion a. relevant structural heart disease (LVH and/or LAE) b. diastolic dysfunction

HF: Heart failure, HFrEF: Heart failure with reduced ejection fraction, HFmrEF: Heart failure with mid-range ejection fraction, HFpEF: Heart failure with preserved ejection fraction, LVEF: Left ventricular ejection fraction, LVH: Left ventricular hypertrophy, LAE: Left atrial enlargement

Table 2: Assessment of hypertension-mediated organ damage[23]

Basic screening tests for hypertension-mediated organ damage
12-lead ECG
Urine albumin: creatinine ratio
Blood creatinine and eGFR
Fundoscopy
More detailed screening for hypertension-mediated organ damage
Echocardiography
Carotid ultrasound
Abdominal ultrasound and Doppler studies
Ankle-brachial index
Cognitive function testing
Brain imaging

ECG: Electrocardiogram, e-GFR: Estimated glomerular filtration rate

Table 3: Patient characteristics that should raise suspicion of secondary hypertension[23]

Characteristic[28]
Grade 2 hypertension in patients <40 years
Hypertension in childhood
Acute worsening hypertension in previously normotensive patients
Resistant hypertension
Hypertensive emergency
Presence of extensive hypertension-mediated organ damage
Features of endocrine abnormalities which cause hypertension
Obstructive sleep apnea
Symptoms/family history of pheochromocytoma

Other causes of secondary hypertension include drugs such as oral contraceptive pills, nonsteroidal anti-inflammatory drugs, herbal remedies, anabolic steroids, nasal decongestants, CNS stimulants, and immunosuppressive medications; and rarer genetic causes such as Liddle syndrome, Gordon syndrome, Geller syndrome, and Glucocorticoid remediable hypertension.

Prevention

Antihypertensive therapy for HF prevention

Clinical trials have shown that the treatment of hypertension reduces the risk of incident HF by up to 64%.[25] Although all anti-hypertensive drugs act to reduce BP, literature shows that not all classes of these drugs have equal propensity to prevent HF.

Beta-blocker therapy which is a cornerstone in HF treatment and has been shown to reduce the risk of mortality and hospital admission in HFrEF patients, has no better preventive effect on HF compared to other antihypertensive drugs. The analysis of 12 randomized controlled trials showed that beta-blockers reduced BP by 12.6/6.1 mm Hg in comparison to placebo, resulting in a 23% reduction in HF risk.[13] However, when compared with other antihypertensive drugs, beta-blockers showed increased risk of stroke in the elderly by 19%, therefore, should not be considered as first-line drugs in older patients.[3,13]

Calcium-channel blockers (CCBs) were initially shown to increase the risk of HF events when compared to diuretics, ACE inhibitors, and angiotensin receptor blockers (ARBs).[3,13] However, a meta-analysis by Thomopoulos *et al*. observed that the anti-hypertensive effect of CCBs is as effective as that of the other anti-hypertensive drugs in the prevention of HF.[26] In addition, CCBs reduce the risk of stroke compared to ACE inhibitors and ARBs, reduce the risk of MI compared to ARBs.[3,13]

Alpha-blockers are not first-line drugs for the treatment of hypertension. In the ALLHAT study, doxazosin showed an increased risk of stroke and doubling of HF risk when compared with chlorthalidone, therefore, indicating that alpha-blockers be avoided as anti-hypertensive drugs in patients who are at risk for or with HF.[13] However, in the ASCOT study, doxazosin was safe and effective when given as a third-line add-on drug, and did not increase the risk of HF.[27]

Renin-angiotensin system blockers are first-line anti-hypertensive drugs and are effective in HF prevention. Between ACE inhibitors and ARBs, no significant difference in efficacy has been documented till present.[3,28,29] Valsartan/sacubitril is the first-in-class angiotensin II receptor neprilysin inhibitor (ARNI), which has shown significant reduction in cardiovascular mortality and morbidity in HFrEF patients, in the PARADIGM-HF trial.[30] This novel drug also has an anti-hypertensive effect and preferentially acts on systolic BP.[31] The anti-hypertensive effect of valsartan/sacubitril is better than that of ARBs.[3]

Thiazide-like diuretics chlorthalidone and indapamide have been proven beyond doubt, to prevent HF when used as antihypertensive drugs. The SHEP trial[32] and the HYVET

trial[33] observed a markedly significant reduction of HF, both with chlorthalidone and indapamide treatment against placebo. Multiple randomized control trials have established the superiority of diuretics in HF prevention as compared to all other antihypertensives.[26] No data for hydrochlorothiazide are available, either for HF or any other cardiovascular endpoint.[3]

To conclude, not all classes of antihypertensive are equal in their efficacy to decelerate the transition from hypertension to HF. Thiazide-like diuretics chlorthalidone and indapamide are preferable over other antihypertensive agents for HF prevention.[3]

Treatment

Treatment of acute hypertensive HF (hypertensive emergency)

This is a clinical condition in which severe hypertension (Grade 3) is associated with acute HF. It is a life-threatening condition requiring immediate but careful intervention to the lower BP, usually with intravenous (i.v.) therapy. The first-line treatment includes i.v. nitroprusside or nitroglycerine with loop diuretic. Alternatively, i.v. urapidil with loop diuretic may be used. Table 5 shows the doses and characteristics of antihypertensive drugs for the treatment of acute hypertensive HF.[16]

Pharmacological therapy for HFrEF

The goals of treatment in patients with HF are to improve their clinical condition, quality of life, prevent hospital admission, and reduce mortality. The recommended treatment for HFrEF consists of neuro-hormonal antagonists, namely, ACEIs, MRAs, and beta-blockers. All these three classes of drugs have been proven to improve survival in patients with HFrEF and are, therefore, recommended for every patient with HFrEF, unless contraindicated, or not tolerated. ARBs have not been consistently proven to reduce mortality in HFrEF patients. Therefore, their usage should be restricted to patients intolerant to ACEI or those who are on ACEI but do not tolerate an MRA.[16]

Valsartan/sacubitril (ARNI) has been proven to be superior to enalapril (ACEI) in reducing cardiovascular mortality and HF hospitalization in HFrEF patients. It is, therefore, recommended as a replacement to ACEI in ambulatory HFrEF patients who are symptomatic despite optimal medical therapy. Ivabradine reduces the elevated heart rate and has been shown to improve outcomes in HFrEF. Ivabradine is recommended in patients with stable symptomatic HF (NYHA Class II–IV) and an LVEF ≤35%, in sinus rhythm and resting heart rate ≥70 bpm despite guidelines-recommended treatment.[16]

Table 4: Common causes of secondary hypertension[23]

Cause	Prevalence in hypertensive patients	Screening investigations
Obstructive sleep apnea	5–10%	Epworth score and ambulatory polygraphy
Renal parenchymal disease	2–10%	Plasma creatinine and electrolytes, eGFR; urine dipstick for blood and protein, urinary albumin:creatinine ratio; renal ultrasound
Atherosclerotic renovascular disease Aortoarteritis	1–10%	Duplex renal artery Doppler; CT angiography or MR angiography
Fibromuscular dysplasia		
Primary Aldosteronism	5–15%	Plasma aldosterone and renin, and aldosterone:renin ratio; hypokalemia (in a minority)
Pheochromocytoma	<1%	Plasma or 24 h urinary fractionated metanephrines
Cushing's syndrome	<1%	24 h urinary free cortisol
Thyroid disease (hyper- or hypothyroidism)	1–2%	Thyroid function tests
Hyperparathyroidism	<1%	Blood levels of parathyroid hormone, calcium
Coarctation of the aorta	<1%	Echocardiogram

eGFR: Estimated glomerular filtration rate, CT: Computed tomography, MR: Magnetic resonance[23]

Table 5: Doses and characteristics of antihypertensive drugs for the treatment of acute hypertensive heart failure[17]

Drug	Onset of action	Duration of action	Dose	Contraindications	Adverse effects
Nitroglycerine	1–5 min	3–5 min	5–200 μg/min i.v. infusion 5 μg/min increase every 5 min		Headache, reflex tachycardia
Nitroprusside	Immediate	1–2 min	0.3–10 μg/kg/min i.v. infusion, increase by 0.5 μg/kg/min every 5 min until goal blood pressure	Liver/kidney failure (relative)	Cyanide intoxication
Urapidil	3–5 min	4–6 h	12.5–25 mg as bolus injection; 5–40 mg/h as continuous infusion		

Sodium–glucose cotransporter 2 (SGLT2) inhibitors are newer class of anti-diabetic drugs which have gained prominence due to their proven benefit in reducing the risk of cardiovascular mortality and HF hospitalization among patients with type 2 diabetes mellitus. The safety and cardiovascular benefit of this class of drugs has recently been established even in HFrEF patients without diabetes mellitus. The DAPA-HF trial demonstrated that dapagliflozin significantly reduced the risk of worsening HF and cardiovascular death in HFrEF patients with NYHA Class II–IV symptoms and LVEF ≤40%, compared to placebo, regardless of the presence or absence of type 2 diabetes mellitus.[34]

Diuretics should be used in HFrEF patients with congestion. Their use should be titrated according to the patient's clinical condition and might be discontinued in selected asymptomatic euvolemic/hypovolemic patients at-least temporarily.[16]

Loop diuretics produce a more intense and shorter diuresis than thiazides and are usually the first line of diuretics used for HFrEF. Together they have a synergistic action and can be combined for treating resistant edema. However, their combination should be used cautiously due to high likelihood of adverse effects.[16]

Hydralazine and isosorbide dinitrate combination may be considered in symptomatic HFrEF patients in whom neither ACEI nor ARB is tolerated, or if they are contraindicated, to reduce mortality.[16]

Table 6 shows the recommended doses of disease-modifying HF medications. The dosage of medications is usually increased every 2–4 weeks as tolerated by the patient, and relevant investigations done periodically, until the maximum tolerated/target dose is achieved. Table 7 shows doses of diuretics commonly used for HF.[16]

Table 6: The recommended doses of disease-modifying HF medications.[16]

Drug – generic name	Starting dose (mg)	Target dose (mg)
ACE-I		
Captopril	6.25 t.i.d.	50 t.i.d
Enalapril	2.5 b.i.d.	10–20 b.i.d.
Lisinopril	2.5–5.0 o.d.	20–35 o.d.
Ramipril	2.5 o.d.	10 o.d.
Trandolapril	0.5 o.d.	4 o.d.
Beta-blockers		
Bisoprolol	1.25 o.d.	10 o.d.
Carvedilol	3.125 b.d.	25 b.i.d. (≤85 kg body weight)
		50 b.i.d. (>85 kg body weight)
Metoprolol succinate	12.5-25 o.d.	200 o.d.
Nebivolol	1.25 o.d.	10 o.d.
ARBs		
Candesartan	4-8 o.d.	32 o.d.
Valsartan	40 b.i.d	160 b.i.d.
Losartan	50 o.d.	150 o.d.
MRAs		
Eplerenone	25 o.d.	50 o.d.
Spironolactone	25 o.d.	50 o.d.
ARNI		
Sacubitril/valsartan	49/51 b.i.d.	97/103 b.i.d.
If-channel blocker		
Ivabradine	5 b.i.d.	7.5 b.i.d.

ACE-I: Angiotensin-converting enzyme inhibitor, ARB: Angiotensin receptor blocker, ARNI: Angiotensin receptor neprilysin inhibitor, b.i.d.: bis in die (twice daily), MRA: Mineralocorticoid receptor antagonist, o.d.: Omne in die (once daily); t.i.d.: ter in die (three times a day)

Treatment of HFpEF

HFpEF is usually associated with concomitant cardiovascular and non-cardiovascular comorbidities, such as COPD, obesity, CKD, CAD, arterial hypertension, AF, anemia, and pulmonary hypertension. Patients with HFpEF are more likely to die or be hospitalized due to non-cardiovascular cause than HF. Therefore, the key to managing these patients also includes treating their comorbidities.[16]

Since no drug has emphatically shown to reduce morbidity or mortality in case of HFmrEF and HFpEF, the focus of treatment is to improve the patients' symptoms.[16]

Diuretics have been proven to improve symptoms across the spectrum of HF. Candesartan, an ARB has shown improvement in NYHA class among patients with LVEF >40% in CHARM-Preserved trial, with a trend toward reduced cardiovascular death and HF hospitalization. Spironolactone and nebivolol might reduce hospitalizations due to HF in HFpEF patients with sinus rhythm. Neuro-hormonal antagonists (ACEIs, ARBs, MRAs, and beta-blockers) have not shown reduction in mortality in HFpEF or HFmrEF patients. Nebivolol, however, has shown reduction in combined endpoint of mortality and HF hospitalization in older patients with HFpEF and HFmrEF.

Recently, the novel drug valsartan/sacubitril (ARNI) has been shown to reduce NT-proBNP and left atrial size in patients with HFpEF.[16]

Antihypertensive therapy in HF patients with persisting hypertension

Lifestyle intervention

Lifestyle intervention is important not only in its ability to BP but also in augmenting the effect of anti-hypertensive therapy.[24] Regular physical activity, cessation of smoking, moderate alcohol consumption, adequate intake of fruits and vegetables, dietary salt restriction, and maintaining ideal body weight are recommended.[1]

Secondary hypertension

The key to managing secondary hypertension lies in treating the primary cause. Interventions addressing the primary cause,

when done at a younger age may be curative. (e.g., renal artery stenting for renal artery stenosis, surgical removal of tumor for pheochromocytoma, and withdrawal of drug/substance in drug induced hypertension). Interventions are less likely to be curative if done later in life, but still, are effective in better control of BP with less medication.[24]

Table 7: The doses of diuretics commonly used in HF[16]

Diuretics	Initial dose (mg)		Usual daily dose (mg)	
Loop diuretics				
Furosemide	20–40		40–240	
Bumetanide	0.5–1.0		1–5	
Torsemide	5–10		10–20	
Thiazides				
Bendroflumethiazide	2.5		2.5–10	
Hydrochlorothiazide	25		12.5–100	
Metolazone	2.5		2.5–10	
Indapamide	2.5		2.5–5	
	Potassium-sparing diuretics			
	+ACE-I/ARB	-ACE-I/ARB	+ACE-I/ARB	-ACE-I/ARB
Spironolactone/eplerenone	12.5–25	50	50	100–200
Amiloride	2.5	5	5–10	10–20
Triamterene	25	50	100	200

ACE-I: Angiotensin-converting enzyme inhibitor, ARB: Angiotensin receptor blocker

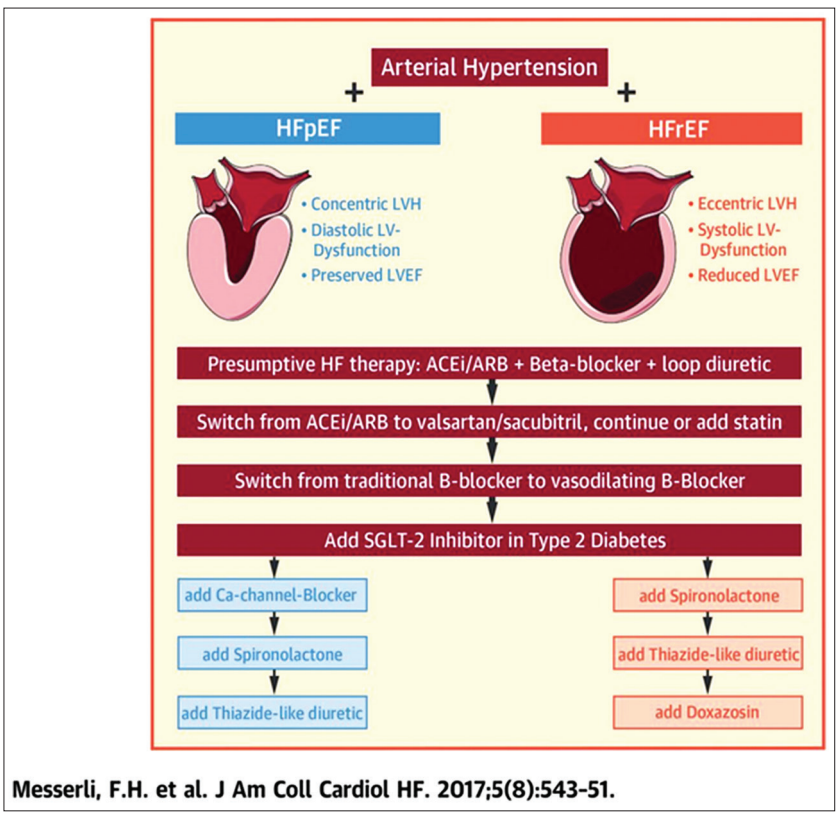

Figure 1: Empirical blood pressure lowering strategy in heart failure with persisting hypertension

Antihypertensive drug therapy

In addition to lowering the BP, the aim of antihypertensive therapy should be to improve systolic function in HFrEF and diastolic function in HFpEF.

If not already initiated, antihypertensive therapy in HFrEF patients should be started when BP is >140/90 mmHg.[24] How low should BP be lowered remains a matter of debate. Due to poor outcomes for HF patients with low BP values, care should be taken so that BP is not actively lowered to <120/70 mmHg.[24] However, patients with the lower BP values should still be continued on guideline-directed HF therapy, as long as it is well tolerated, due to its protective effect.[35]

The recommended drugs for the treatment of hypertension in HFrEF patients include guideline-directed HF medications.[35] They include ACE inhibitors, ARBs, MRAs, and beta-blockers, all of which have been convincingly proven to be effective in improving clinical outcome in HFrEF patients. The benefit of diuretics in HF patients is restricted to alleviating symptoms.[24]

Valsartan/sacubitril lowers BP and improves clinical outcomes in HFrEF patients, and is recommended in the treatment of HFrEF as an alternative to ACE inhibitors or ARBs.[30] As a first step toward better after-load reduction, these patients may be switched to valsartan/sacubitril.

In addition, a vasodilating beta-blocker such as carvedilol or nebivolol may be preferred to other beta-blockers for better BP control.[3] A dihydropyridine CCB may be used if further BP reduction is needed.

Centrally acting agents such as clonidine and non-dihydropyridine CCBs are not to be used.[24]

SGLT2 inhibitors have consistently shown a modest reduction in systolic and diastolic BP.[36] These newer class of drugs exert their BP lowering effect by osmotic diuresis and have been reported to be especially useful in some cases of resistant hypertension in diabetic patients.[37]

In case of HFpEF patients requiring antihypertensive therapy, the same strategy followed for HFrEF patients might be applied.[24] Threshold for starting BP lowering therapy and target BP values for HFpEF patients are same as for HFrEF.[35] Statin therapy is important in HFpEF patients for reducing microvascular dysfunction.[3]

Based on clinical and pathophysiologic features, Messerli *et al*. have suggested the following BP lowering strategy in HF with persisting hypertension [Figure 1].[3]

Conclusion

Hypertensive heart failure is an important manifestation of HMOD and carries a poor prognosis if not treated promptly and adequately. Patients should be investigated for other manifestations of HMOD and secondary causes of hypertension, and treated accordingly. Optimal BP control is vital in prevention of HMOD, including HF. Thiazide-like diuretics namely chlorthalidone and indapamide, and RAAS (renin-angiotensin-aldosterone system) blockade by ACE-I/ARBs are effective in HF prevention compared to other antihypertensive drugs. Acute hypertensive HF is a life threatening emergency which requires immediate treatment with intravenous BP lowering therapy. In chronic and more stable patients, guideline directed HF medical therapy including ACE-I/ARB/ARNI, MRA, beta-blockers are recommended for BP reduction. Dihydropyridine CCBs and thiazide-like diuretics can be used in addition to the above drugs for better BP control. Diuretics are useful for symptomatic relief across the spectrum of HF. Special attention should be paid to management of concomitant cardiovascular and non-cardiovascular comorbidities in HFpEF patients to improve outcomes. SGLT2 inhibitors provide remarkable cardiovascular benefit and modest BP reduction in HFrEF patients with and without diabetes, when given in addition to GDMT.

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