Hypertension and Heart Failure
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Abstract

Background: Hypertension is the leading cause of heart failure worldwide leading to adverse cardiovascular outcomes. However, little is known about the target blood pressure goals in patients with heart failure. Body: Chronic hypertension leads to the left ventricular hypertrophy and further remodeling may cause heart failure with preserved ejection fraction and eventually heart failure with reduced ejection fraction. Various societal guidelines have come forward to decide on target blood pressure goals in specific high-risk populations. However, only some evidence is available on target blood pressure goals in heart failure patients and most of these data have been extrapolated from other studies. With the data currently available, treating hypertension at a level of 140/90 mmHg and titrating to 130/80 mmHg in patients with heart failure looks well justified. However, targeting blood pressure below 120/70 mmHg remains a gray zone and should ideally be avoided. Conclusion: Further prospective studies are needed to define target blood pressure goals in patients with heart failure.

Key words: Heart failure, Hypertension, J Curve

Introduction

Hypertension is defined as blood pressure above 140/90 mmHg and is a leading cause for the development of heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF).[¹] Although equally prevalent in both the forms of heart failure, it remains more common in HFpEF patients with prevalence of up to 90%, compared to HFrEF.[²,³] Various guidelines have recommended not only different staging systems for hypertension but also the target blood pressure (BP) goals and therapeutic drug usage in specified populations. Although the target BP goals and therapeutic strategies for BP control in HF patients have been mentioned in different guidelines, robust data are still lacking. Most of the recommendations for optimal BP control in HF patients have been extrapolated from other high-risk populations where intensive BP control showed better long-term cardiovascular (CV) outcomes, however, at an increased risk of adverse effects. Chronic hypertension causes pressure overload leading to ventricular hypertrophy which is initial compensatory mechanism and preserves cardiac output. Subsequently, the left ventricle (LV) dilates as remodeling occurs and LV starts to decompensate. Remodeling occurs due to activation of renin-angiotensin system, sympathetic nervous system, and deposition of extracellular matrix. Diastolic dysfunction or the so-called HFpEF is the primary manifestation of hypertensive heart failure. It is only in the later stages that dilated cardiomyopathy leading to HFrEF sets in. Long-term prognosis is poor with increased mortality in hypertensive patients with HF. Treating hypertension can significantly reduce incident of HF and HF hospitalization, especially in old population.[⁵,⁶]

Prevalence of Hypertension in Patients with Heart Failure

The Framingham Heart Study, which involved 5,143 patients (20 years follow-up) showed that the hypertension precedes the progression of heart failure among 91% newly diagnosed heart failure patients. Male and female cohorts showed 2- and 3-fold increase risk of developing heart failure, respectively, compared to normotensive individuals.[⁸] The Korean Heart Failure (KorHF) study (2004–2009) recruited 3,200 patients with HF...
and showed that 36.7% of the patients had hypertensive HF.\textsuperscript{[9]} ATTEND registry (2002–2011) conducted in Japan with 4842 patients suggested that majority of hospitalized heart failure patient are the elderly with either new-onset hypertension or a history of hypertension (overall 70% were hypertensive).\textsuperscript{[10]} In KorAHF study (2011–2014), 62% of patients had a history of hypertension, however, only 4% decompensation were attributed to hypertension.\textsuperscript{[11]} ESC-HF-LT (2011–2013) registry involving 12,440 subjects suggested the coexistence of hypertension and heart failure among 65.6% of patients.\textsuperscript{[12]} Similarly, ASIAN-HF showed 55.4% coexistence of heart failure and hypertension.\textsuperscript{[13]} The ADHERE registry (2002–2004) registry, involving 1,59,168 subjects, suggested that 69% of subjects with heart failure with reduced ejection fraction and 77% of the subjects with heart failure with preserved ejection fraction had hypertension.\textsuperscript{[14]} However, contrary to other studies, ADHERE registry showed that almost 30% of the acute decompensation were caused by hypertension and this was more common in patients with preserved ejection fraction.

**Why We Need Optimal BP Control in HF Patients?**

There is clear evidence for linear association between hypertension and cardiovascular event in the general population. However, association between blood pressure and clinical outcomes in HF patients is poorly understood, which creates a challenge in managing them. The J curve effect reflects an inverse relationship between low blood pressure and cardiovascular outcomes. This effect is seen predominantly in patients with preexisting coronary artery disease (CAD) and hypertension and does not appear in stroke or renal disease as the coronaries are perfused during diastole, whereas the renal arteries and carotids are perfused in systole. However, as most of the data are derived from trials without HF patients, it is difficult to extrapolate the existence of J-shaped curve and optimal blood pressure for HF patients. J shape relationship between systolic blood pressure (SBP) and diastolic blood pressure (DBP) with all-cause and cardiovascular mortality among HF patients has been demonstrated in observational study. That means cardiovascular events may increase at both too high and too low levels of blood pressure. One of the observational studies demonstrated that at a nadir of SBP/DBP of 132/74 mm of Hg, there was a reverse J association between on treatment BP and long-term mortality in HF patients. This suggests that the too low BP can be actually harmful for the HF patients and cannot be considered optimum target.\textsuperscript{[14,15]} Low BP might be related to severe LV dysfunction and low cardiac output which are actual causes for the adverse clinical outcome rather than BP itself. This is supported by evidence for resynchronization therapy which demonstrated significant increase in BP and reduced in mortality and HF hospitalization in patients with lower baseline BP which improved due to device-related improvement in cardiac function. Whether the relationship between SBP and mortality in HF patients follows a linear or non-linear trend is still controversial.\textsuperscript{[15,19]}

**Guideline-recommended Treatment for Hypertension in HF**

Many randomized controlled trials (RCTs) and guidelines exist currently for the management of arterial hypertension including European Society of Cardiology (ESC) 2018 hypertension guidelines, American College of Cardiology/American Heart Association (ACC/AHA) 2017 hypertension guidelines, and International Society of Hypertension (ISH) 2020 guidelines.\textsuperscript{12,20,21} Although the drugs used in all these guidelines remain the same, there may be subtle alterations in step-wise management. There are no RCTs comparing the different antihypertensive drugs and treatment goal in HF patients. Most of the data existing are from the heart failure trials and guidelines where these drugs have shown mortality benefits in patients with HFrEF. All recommendations have been derived from other trials in which intensive BP reduction showed significant benefit in CV outcomes. This suggests BP reduction if the baseline BP \( \geq 140/90 \text{ mmHg} \), similar to general population without HF. However, ideal BP target in HF has not been studied in RCTs.\textsuperscript{[12]}

**Target BP in Patients with HFrEF and HFpEF**

No RCTs have been done in patients with hypertension and heart failure to evaluate the ideal BP targets. Hence, the current recommendations are based solely on the expert consensus. According to major guidelines, target SBP of \( <130 \text{ mmHg} \) in HFrEF and HFpEF patients on the basis of systolic blood pressure intervention trial (SPRINT) trial is recommended. The trial compared intensive BP control to standard BP control. However, it was prematurely terminated at 3 years as intensive BP group showed superiority in the form of primary outcome of CV event, stroke, HF, and CV mortality. However, it is not justifiable to extrapolate the results of SPRINT trial to HF patients as the trial had excluded HF patients with EF less than 35% or who had symptomatic heart failure 6 months before enrollment.\textsuperscript{[12,20,21]} Apart from this, these targets might have been formulated from trials where other high-risk population were studied such as coronary artery disease, peripheral vascular disease, stroke or TIA, and diabetes mellitus\textsuperscript{22-28} [Figure 1].

The 2017 ACC/AHA/Heart Failure Society of America (HFSA) guidelines for the management of HF have recommended a BP goal of \( <130/80 \text{ mmHg} \), whereas the American Academy of Family Physicians (AAFP), the American College of Physicians (ACP), and the ESC HF guidelines have opted not to follow an intensive BP target of \( <130/80 \text{ mmHg} \).\textsuperscript{[29]} According to ESC 2018 hypertension guidelines, in patients with HFrEF, BP should be lowered if baseline BP is \( \geq 140/90 \text{ mmHg} \). However, it remains a matter of debate how low the BP should be lowered in HF patients. However, as per most of the published data, outcome for HF patients with BP \( <120/70 \text{ mmHg} \) remains poor.\textsuperscript{[12,24]} [Figure 2].

HFrEF patients commonly have multiple comorbidities and that may adversely affect outcome and complicate management. Same BP threshold and drugs used for HFrEF are advised for HFpEF.\textsuperscript{12,20,21}
Management of Hypertension in Patients with HFrEF and HfPEF

Most of the drugs which are approved in guideline directed medical therapy of HFrEF such as angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs), beta-blockers, angiotensin receptor neprilysin inhibitors (ARNIs), and mineralocorticoid receptor antagonists (MRAs) have potential to reduce BP. However, this CV benefit is
directly related to BP reduction or not is still controversial.[31-36] Antihypertensive medication is commonly needed for HFpEF patients but optimum strategy is unknown. Till date, no drug has clearly shown benefit in the form of decrease in morbidity and mortality in HFpEF patients. Hence, optimal therapy remains symptomatic improvement and improving quality of life. Reduction in BP can lead to the regression of the left ventricular hypertrophy (LVH), accompanied by a reduction of CV events and mortality. ACE/ARB and CCB are more effective for LVH regression than beta-blockers or diuretics.[39-41] Although evidence for the management of HTN in HFpEF is limited, guidelines recommend RAAS blocker such as ACEI/ARBS as first-line drugs.[42-45]

Management of Hypertension in Special Population

Hypertension should not only be seen as a comorbid condition which can present with HFpEF but the management of hypertension in other comorbid conditions which can present with heart failure deserves a mention. This special population includes advanced age, patients with chronic kidney disease (CKD), patients with diabetes mellitus, and patients with atrial fibrillation.[46] In patients with advanced age, optimal BP control not only reduces the chances of major events such as intracranial hemorrhage and cerebral infarction but may also reduce the risk of dementia. One should ideally aim for conservative targets like SBP <140 mmHg and avoid achieving intensive goals. In patients with diabetes mellitus, ACEIs/ARBs remain to be the first-line therapy in view of their ability to regress left ventricular hypertrophy and prevent the progression of microalbuminuria. In patients with chronic kidney disease, ACEIs/ARBs remain the first-line therapy (when not contraindicated) along with dihydropyridine CCB. Hypertension remains to be an important risk factor for the development of atrial fibrillation and minimum three blood pressure recording should be for accurate diagnosis and treatment. Beta-blockers and non-dihydropyridine CCB are recommended for rate control in AF with fast ventricular rate, however, latter should be avoided in patients with HFrEF.

Summary

Uncontrolled hypertension beyond a threshold of 140/90 mmHg is clearly associated with an increase in long-term risk of adverse events in the general population. Data on the effect of hypertension and benefit from treatment on the long-term outcomes in heart failure are primarily extrapolations from studies that excluded patients with heart failure. Further thoughtfully designed and adequately powered studies are required to determine optimal targets for blood pressure reduction in heart failure (HFrEF as well as HFpEF). At present, however, major societal guidelines recommend a threshold of 140/90 mmHg for initiation of treatment in heart failure as well. A systolic blood pressure of 130 and diastolic of 80 mm of Hg should be targeted. Lowering beyond a blood pressure of 120/70 must be accompanied by a risk–benefit analysis and may be considered if further drug therapy is necessary to improve the overall prognosis in patients with heart failure.

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