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Short CV

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Dr. Faselis received his medical degree from the University of Athens School of Medicine and completed his residency in Internal Medicine at Cook County Hospital and Medicine Fellowship at the University of North Carolina. Prior to being appointed the Chief of Staff, Dr. Faselis served as the Chairman of Medicine and the Chief Academic Officer and Dean for Veterans Academic Affairs.

Επίκαιρο Άρθρο

Systolic Blood Pressure and Mortality in Heart Failure: How Low to Go?

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ABSTRACT

The management of heart failure presents several challenges in daily clinical practice. Among these is blood pressure (BP) control which has been an issue of debate over the years. While a linear relation between BP levels and cardiovascular morbidity and mortality has been identified in the general population, in heart failure (HF) patients data are inconclusive. Several studies point toward a J-shape relation between systolic BP and morbidity and mortality. Specifically, both systolic BP levels less than 100-110 mmHg and higher than 130 mmHg were shown to be associated with increased risk for death. While the latter is anticipated based on data from the general hypertensive population, the association between low systolic BP and outcomes raises several questions. It is still unclear whether low BP levels are the cause of the observed increased risk for mortality or a marker of poorer health and cardiac function, which consequently result in death. Prospective studies with long-term follow-up periods addressing the association of BP levels with morbidity and mortality outcomes are urgently needed to unveil the optimal BP levels goals in all HF subclasses.

Key-words: heart failure; blood pressure; target blood pressure; hypertension; mortality.

Introduction

The prevalence of arterial hypertension ranges from 20%-70% in studies of patients with heart failure (HF)[1,2], and is higher in patients with preserved ejection fraction (EF) than in patients with reduced EF, with a prevalence of up to 90% in the former[3-5].

Various drugs with antihypertensive action are commonly used in HF patients, such as renin-angiotensin system inhibitors, mineralocorticoid antagonists, angiotensin receptor-neprilysin inhibitors, beta-blockers and even sodium-glucose co-transporter 2 inhibitors[6-10]. All the above were shown to offer cardiovascular protection in patients with HF and reduced EF. On the contrary such drug-related benefits may not be observed in patients with preserved EF[6-10].

However, these benefits may not be associated with the BP-lowering effect of the drugs per se. In contrast to the well-established linear relation of BP levels and cardiovascular outcomes in the general population, the association between BP levels and morbidity and mortality outcomes in patients with HF has been an issue of debate over the years[11,12]. Importantly, studies reported a J-shape relationship between systolic BP and all-cause mortality in the setting of HF, especially in patients with reduced EF[11,12].

Systolic BP and outcomes

Several studies have examined the relation between systolic BP and morbidity and mortality. In general, it has been demonstrated that low BP levels are associated with increased mortality in patients with

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HF[11,12]. In more than 5.700 patients with New York Heart Association (NYHA) class II or III HF and EF less than 0.45, all-cause mortality rate during the entire study period for patients with a baseline systolic BP lower than 100 mmHg was 50%, significantly higher compared to patients with systolic BP levels of 130 to 139 mm Hg (mortality rate of 32%)[13]. In another study assessing the relation between baseline BP levels and mortality outcomes, it was reported that in more than 7.200 patients with mild to moderate chronic systolic and diastolic HF, systolic BP levels lower than 120 mmHg were related with a higher CV and HF mortality by 15% and 30%, respectively after 5 years compared to patients with a systolic BP greater than 120 mmHg. Importantly, all-cause death did not differ significantly between the two groups[14]. A meta-analysis of 10 studies of more than 8.000 patients with chronic HF found a decrease in mortality of 13% with an increase in systolic BP of 10 mmHg. The effect of a higher systolic BP was most noticeable in populations with a lower starting SBP, with an 18% lower mortality in the lowest tertile (patients with mean systolic BP of 109 mmHg)[15].

Another study assessed the relation between discharge systolic BP and all-cause mortality among 6.778 hospitalized patients with HF with preserved EF and hypertension from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure registry. It was found that a target systolic BP lower than 130 mmHg was not associated with increased mortality compared to patients with systolic BP greater than 130 mmHg. However, a systolic BP less than 120 mmHg was related with a significantly higher mortality of 68%, 28% and 11% after 30 days, 12 months and 6 years of discharge compared to patients with systolic BP greater than 130 mmHg. Importantly, the risk for hospital readmission was similar across all BP groups[16].

The theory that low systolic BP may be associated with increased risk for mortality is further supported by studies of cardiac devices, in which resychronization therapy significantly increased BP levels and reduced the mortality and HF hospitalization risk, a benefit that was more evident in patients with low BP levels before treatment in whom BP increased significantly with cardiac resynchronization[17].

Apart from systolic BP levels, BP variability was also shown to be associated with incased risk for morbidity and mortality. Among 7.453 patients with chronic HF, the highest mortality was observed in patients with systolic BP lower than 90 mmHg compared to patients with a systolic BP greater than 130 mmHg. Patients with BP levels between 90 to 129 mmHg demonstrated an in-between risk. BP variability was associated with death or heart transplantation. An increase or decrease greater than 10 mmHg per year resulted in a significantly 80% and 2-fold risk increase, respectively for death or heart transplantation[18].

The crucial question is how low systolic BP can be reduced. In contrast, to other populations were the nadir point seems to range between 100 to 120 mmHg of SBP, the limited findings in HF patients suggest that the nadir point is at higher BP levels. In a study of more than 5.600 patients with acute HF who were followed for 2 years after discharge, a nadir point of 132.4 for systolic and 74.2 mm Hg for diastolic BP was observed when the event rate was the lowest. Specifically, it was shown that the event rate increased significantly below and above the reference BP range (130-140 / 70-80 mmHg), except for patients with BP above the reference BP range, where an insignificant trend for increase in mortality was found above 150 mmHg. The J-curve relationship was observed in both patients with reduced and preserved EF for all-cause mortality, with the lower risk at 136.0 / 76.6 mmHg and 127.9 / 72.7 mmHg, respectively. Mortality risks increased significantly at lower and higher BP levels for both systolic and diastolic BP in patients with HF and preserved EF. In contrast, mortality rates were significantly elevated only at lower BP groups, whereas a trend for an increase was found at higher systolic BP levels groups of HF patients with reduced EF[19].

Low BP and mortality: a cause or a sign?

It is still a matter of great debate whether there is a causal relationship between low BP levels and increased risk for morbidity and mortality events. Low BP levels result in tissue hypoperfusion, deterioration of cardiac function and increased events. On the other hand, it may be that other conditions are directly responsible for the increased mortality and at the same time cause low BP (such as cancer and renal disease)[20-22], and thus reverse causality could result in increased mortality rates. In addition, patients with more severe forms of cardiac dysfunction are commonly found with low systolic BP, suggesting higher risk for events[23,24]. Low diastolic BP could be an indication of progressed vascular disease and ar-

terial stiffness, conditions that result in higher risk for cardiovascular morbidity and mortality. Thus, low diastolic BP may result in limited perfusion of the already sclerotic coronary arteries, increasing the risk for coronary events[25-27].

Guidelines recommendations

Due to unavailable and sufficient data, international guidelines are currently reluctant to suggest aggressive BP level goals in patients with HF. The 2018 European Society of Hypertension / European Society of Cardiology hypertension guidelines suggest an upper threshold BP of 140/90 mmHg and to avoid reducing BP lower than 120/70 mmHg in both patients with reduced and preserved EF, unless patients tolerate low BP levels or a more aggressive BP reduction is needed for reasons other than BP[28]. The American guidelines for the management of Hypertension suggest an upper threshold of 130/80 mmHg and target BP of less than 130/80 mmHg. However, they state that relevant trials in HF are missing and caution is advised[29] when lowering BP in these patients. Similar recommendations come from the American HF guidelines[30], whereas the European HF recommendations suggest BP targets similar to the ones for the general population[31].

Conclusion

Currently, studies assessing the impact of systolic BP and morbidity and mortality outcomes are scarce. Existing evidence suggest that both low (less than 100-110 mmHg) and increased (greater than 130-140 mmHg) BP levels may be related with worse outcomes. Prospective studies with long-term follow-up periods addressing the association of BP levels with morbidity and mortality outcomes are urgently needed to unveil the optimal BP levels goals in patients with preserved, mid-range and reduced EF.

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