J’ Curve and Blood Pressure: Recent Insight?

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INTRODUCTION

W e have enough evidences that uncontrolled hypertension increases cardiovascular morbidity and lowering elevated BPs can reduce such events. The question that now arises is to what level should the BP be lowered to optimize treatment? Lower the better has been a dictum for most of the physicians over the last few decades. But recently some data have emerged which focused on the dangers of lowering BP below certain levels. That is how the concept of a J-shaped curve relationship between BP and cardiac morbidity and mortality has emerged.

What is a J curve relation between BP and CAD: When the elevated BP, is lowered, the cardiovascular events decreases initially but lowering BP below a critical point is no longer beneficial and possibly even deleterious thus forming a J curve (See figure-1).

History of Hypertension: The term hypertension was derived from a greek word ‘essentielle Hypertonie’ meaning there is some increase in the tone of arteries which is essential to serve oxygenated blood to the vital organs. So the elevation of BP was considered a natural response to guarantee a more normal circulation to the heart, brain and kidneys. There was a fear in the mind of physicians that lowering BP might compromise vital organ perfusion. This concept remained viable for decades. Gradually the people started realizing that raised BP can cause serious harm and it should be brought down to a normal level. Than a school of thought came that the more lower you bring down the BP, the better it is. Thus the pendulum began to swing from one extreme (elevated BP considered essential for vital organ perfusion), to the other extreme, “the lower the better,” Now the J curve stands in between the two extremes.

Mechanism of J curve: Coronary circulation, unlike all other circulation receives its blood supply mainly in diastole. If the diastolic BP is reduced beyond a certain level it may compromise coronary flow which can lead to acute coronary ischemia. This is more prevalent particularly in the presence of pre existing coronary artery disease and left ventricular hypertrophy. (see figure -2)

Evidences in favour of J curve: The question was not whether there was a J-curve-obviously there has to be, because a BP of 0 encompasses a 100% mortality. But the real question was, whether such a J-curve did occur within a “physiologic” range of BP.

Numerous studies have documented an inverse relationship
between DBP and coronary heart disease (i.e., a J-shaped curve)\(^{10-18}\). In most studies, the J-shaped curve was found to be in the physiologic range at levels of DBP below 70 to 80 mm Hg. The HOT study-in which 18,790 patients were titrated to target DBPs of below 90, below 85, and below 80 mm Hg-documented a J-shaped curve in the 3,000 patients with coronary heart disease in whom the frequency of cardiovascular events/1,000 patient-years was roughly twice as high compared with the non ischemic group. Thus, the HOT study establishes a J-curve relationship between DBP and the risk of MI in patients with documented coronary heart disease\(^{19-20}\). The 22,576-patient INVEST study was an ideal model to analyze the significance of the J-curve, because all patients had CAD and hypertension\(^{21}\). Indeed, the primary outcome in the INVEST study doubled when DBP was below 70 mm Hg and quadrupled when it was below 60 mm Hg. The nadir for DBP was 84 mm Hg.

**J curve is different subsets of patients**

*a. J curve in patients with and without preexisting CAD:* Patients with hypertension and IHD have a limited coronary flow reserve (virtually zero if coronary stenosis is 85% or greater, particularly in the presence of LVH or increased heart rates), so excessive lowering of DBP results in a fall in coronary flow with no sizeable compensatory increase in oxygen extraction; such events increase the risk of an MI\(^{22}\). J curve is more prevalent in hypertensive patients with pre-existing CAD than those without CAD as shown in the study by …… (fig-3)

*b. Diabetics with hypertension?* American diabetic association states that there is no threshold value for hypertension and risk continues to decrease well into the normal range\(^{23}\). JNC-VII guideline states that diabetic should have a BP of <130/80 mm Hg\(^{24}\). However evidence supporting such statement is lacking. In the recent ACCORD trial 4733 diabetic patients were randomly assigned to a SBP target lower than 120mmHg or lower than 140 mmHg\(^{25}\). The mean follow-up was 4.7 years. Despite achieving a significantly lower SBP in the intensive treatment group, there was no significant difference in the primary combined outcome (nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes). However, there was a 2% increase in absolute risk in serious adverse events attributed to antihypertensive treatment in the intensive therapy group. So ‘lower the better’ strategy cannot be applied to all diabetics with hypertension.

*c. Chronic Kidney Disease and Hypertension:* In
observational studies, the relationship between BP and the progression of chronic kidney disease or incident ESRD is direct and progressive. Yet few trials have tested the effects of intensive blood-pressure control, as compared with traditional control, on the progression of chronic kidney disease, and the findings from such trials have been inconsistent. Despite a lack of compelling evidence, numerous guidelines have recommend a reduced BP target in patients with chronic kidney disease. In a recent AASK study 1094 black patients with hypertensive chronic kidney disease were randomized to receive either intensive (<130/80 mm Hg) or standard blood-pressure control (<140/90 mm Hg). In overall analyses, intensive blood-pressure control had no effect on kidney disease progression (hazard ratio in the intensive-control group, 0.91; P = 0.27). However, the effects differed according to the baseline level of proteinuria (P = 0.02 for interaction), with potential benefit in patients with a protein-to-creatinine ratio of more than 0.22 (hazard ratio, 0.73; P = 0.01). So lower the better strategy cannot be applied to all CKD patients with hypertension but only to a subset of patients with significant proteinurea. However we need more trial in this issue.

d. J curve in relation to stroke: Though an inverse relation has been seen between DBP and CAD but this statement does not seem to hold true for cerebrovascular disease. In the INVEST study, there was a significant and progressive preponderance of MIs over strokes at low DBP values. Also in the ACCORD study the intense BP reduction arm has a significantly less incidence of stroke than the standard arm. So the relation of BP reduction and risk of stroke is linear and not a J curve.

e. J curve and isolated systolic hypertension: It has been suggested that low diastolic BP (BP) while receiving antihypertensive treatment is harmful in older patients with systolic hypertension. These findings support the hypothesis that antihypertensive treatment can be intensified to prevent cardiovascular events when systolic BP is not under control in older patients with systolic hypertension, at least until diastolic BP reaches 55 mm Hg. However, a prudent approach is warranted in patients with concomitant coronary heart disease, in whom diastolic BP should probably not be lowered to less than 70 mm Hg.

CONCLUSION

There are number of studies which have shown an inverse relationship between DBP and coronary heart disease (i.e., a J-shaped curve). In most studies, the J-shaped curve was found to be in the physiologic range at levels of DBP below 70 to 80 mm Hg. J curve concept is more valid in patients who have CAD than those who do not have. J curve does not exist for stroke patients in which lower is still better. Recent data have shown that even in diabetics and CKD patients very intense BP control is not superior to standard control. Finally the fear of J curve should not deter practicing physicians from pursuing more aggressive control in treating hypertension, because currently, at best, only approximately one-third of our patients are at goal BP of 140/90 mm Hg.

Fig. 4: Incidence of MI and stroke by DBP in the INVEST study

REFERENCES
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