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## From Journal of the American College of Cardiology The J-curve between Blood Pressure and Coronary Artery Disease or Essential Hypertension: Exactly How Essential?



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### Abstract and Introduction

#### Abstract

The topic of the J-curve relationship between blood pressure and coronary artery disease (CAD) has been the subject of much controversy for the past decades. An inverse relationship between diastolic pressure and adverse cardiac ischemic events (i.e., the lower the diastolic pressure the greater the risk of coronary heart disease and adverse outcomes) has been observed in numerous studies. This effect is even more pronounced in patients with underlying CAD. Indeed, a J-shaped relationship between diastolic pressure and coronary events was documented in treated patients with CAD in most large trials that scrutinized this relationship. In contrast to any other vascular bed, the coronary circulation receives its perfusion mostly during diastole; hence, an excessive decrease in diastolic pressure can significantly hamper perfusion. This adverse effect of too low a diastolic pressure on coronary heart disease leaves the practicing physician with the disturbing possibility that, in patients at risk, lowering blood pressure to levels that prevent stroke or renal disease might actually precipitate myocardial ischemia. However, these concerns should not deter physicians from pursuing a more aggressive control of hypertension, because currently blood pressure is brought to recommended target levels in only approximately one-third of patients.

#### Introduction

The term "essential hypertension" was coined by Frank<sup>[1]</sup> almost a century ago by stating "Because in this disease the increase in tone of the small arteries in the whole body (which leads to an increase in blood pressure) is the primary event...I will, in the following, name this disease, essential hypertension (essentielle Hypertonie)." The concept of hypertension being essential (i.e., serving to force blood through sclerotic arteries to the target organs) remained alive and well into the 1970s, and statements like "For aught we know, the hypertension might be a compensatory mechanism that should not be tampered with even were it certain that we could control it"<sup>[2]</sup> and "May not the elevation of blood pressure be a natural response to guarantee a more normal circulation to the heart, brain and kidneys"<sup>[3]</sup> continued to appear in published reports and spook physicians. This concept also instigated fear that, in susceptible patients, blood pressure (BP) could be lowered too much. Hence, the reluctance of many physicians to expose patients to antihypertensive therapy is not surprising, because abrupt lowering of BP in hypertensive emergencies, paradoxically, can increase target organ disease such as renal failure, encephalopathy, and coronary ischemia and even directly cause heart attacks, stroke, and death.<sup>[4]</sup> Gradually, however, the pendulum began to swing toward the other extreme, and the dictum, "the lower the better," became the leitmotiv for most physicians treating hypertension. The large, thorough meta-analysis of Lewington et al.<sup>[5]</sup> corroborated and amplified this concept by stating that "usual BP is strongly and directly related to vascular (and overall) mortality without any evidence of a threshold down to at least 115/75 mm Hg." Statements like these threatened to put an end to the "essentiality" of essential hypertension.

## The J-curve Concept

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Aggressive BP-lowering notwithstanding, a concept that never quite vanished from the published reports and surfaced in many randomized trials was the J-curve phenomenon. The question was not whether there was a J-curve—obviously there had to be, because a BP of 0 encompasses a 100% mortality—the question was whether such a J-curve did occur within a "physiologic" range of BP. Because the coronary arteries are perfused predominantly during diastole, a J-curve, if any, should be most apparent for diastolic pressure and coronary events.

Three decades ago Stewart<sup>[6]</sup> cautioned against too-aggressive antihypertensive therapy, because cardiovascular complications might be increased with a fall in BP, especially diastolic blood pressure (DBP). On comparing the DBP of 169 hypertensive patients taking antihypertensive agents over a 6-year period, a DBP of <90 mm Hg was associated with a 5-fold greater risk of myocardial infarction (MI) compared with a DBP of 100 to 109 mm Hg.<sup>[6]</sup> One decade later, Cruickshank et al.,<sup>[7]</sup> in 902 patients with moderate-to-severe hypertension, reported a strong J-curve relationship between death from MI and treated DBP only in patients with coronary artery disease (CAD). The nadir of the J-curve in DBP was at 85 to 90 mm Hg, with an increase of mortality from MI on either side of this range. In patients without CAD, there was no J-curve or J-curve relationship with systolic pressure in those with or without CAD. In 1992, Farnett et al.<sup>[8]</sup> thoroughly analyzed a series of large hypertension studies and demonstrated a consistent J-shaped relationship for cardiac events and DBP but not between treated BP and stroke or systolic pressure and cardiac events. Emphasizing the organ-specific effect of low DBP, the authors commented that this might "leave a clinician with the uncomfortable choice of whether to prevent stroke or renal disease at the expense of coronary heart disease or vice versa."

## Pathophysiologic Consideration: Coronary Flow and BP

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The coronary circulation is unique in that most of coronary blood flow to the left ventricle (LV) occurs in diastole. During systole, the contracting LV myocardium compresses intramyocardial vessels and obstructs its own blood flow. At peak systole, there is even a backflow in the coronary arteries, particularly in the intramural and small epicardial arteries.<sup>[9]</sup> Coronary perfusion pressure is the pressure gradient between the coronary arteries and the right atrium or LV in diastole. When coronary perfusion pressure is lowered to 40 to 50 mm Hg, the so-called pressure at 0 flow, diastolic blood flow in the coronaries ceases.<sup>[10]</sup>

Normal epicardial coronary arteries are conductance vessels and do not offer any significant resistance to blood flow. Even at the highest level of blood flow, there is no detectable pressure drop along the length of human epicardial arteries.<sup>[11]</sup> These arteries branch into a series of arterioles in which a larger pressure drop occurs. The arterioles then arborize into a dense capillary network of approximately 4,000/mm<sup>2</sup> to ensure that each myocyte is adjacent to a capillary. This capillary density is reduced in the presence of left ventricular hypertrophy (LVH). There is no functional evidence of enhanced coronary collateral circulation in patients with LVH as was previously believed.<sup>[12]</sup>

Autoregulation ensures relatively constant myocyte perfusion over a wide perfusion pressure range of 45 to 125 mm Hg.<sup>[13]</sup> It follows that autoregulation will compensate for the various degrees of proximal epicardial coronary obstruction, ensuring optimal distal blood flow to the myocytes. However, in patients with CAD, autoregulation can be compromised. A fall in DBP might lower perfusion pressure distal to a stenosis below the critical level at which autoregulation is effective, thereby compromising myocardial perfusion, intensifying myocardial ischemia, and causing an increase in LV filling pressures, which in turn further reduces the perfusion gradient. Longstanding hypertension and LVH narrow the range of coronary arterial autoregulation, especially in the subendocardium.<sup>[14]</sup> In patients with LVH, subendocardial ischemia might occur even in the absence of stenosis. It follows that a DBP range considered to be "physiologic" might precipitate the vicious cycle of myocardial ischemia and infarction in patients with compromised coronary flow and concomitant LVH.

## Effect of BP-lowering

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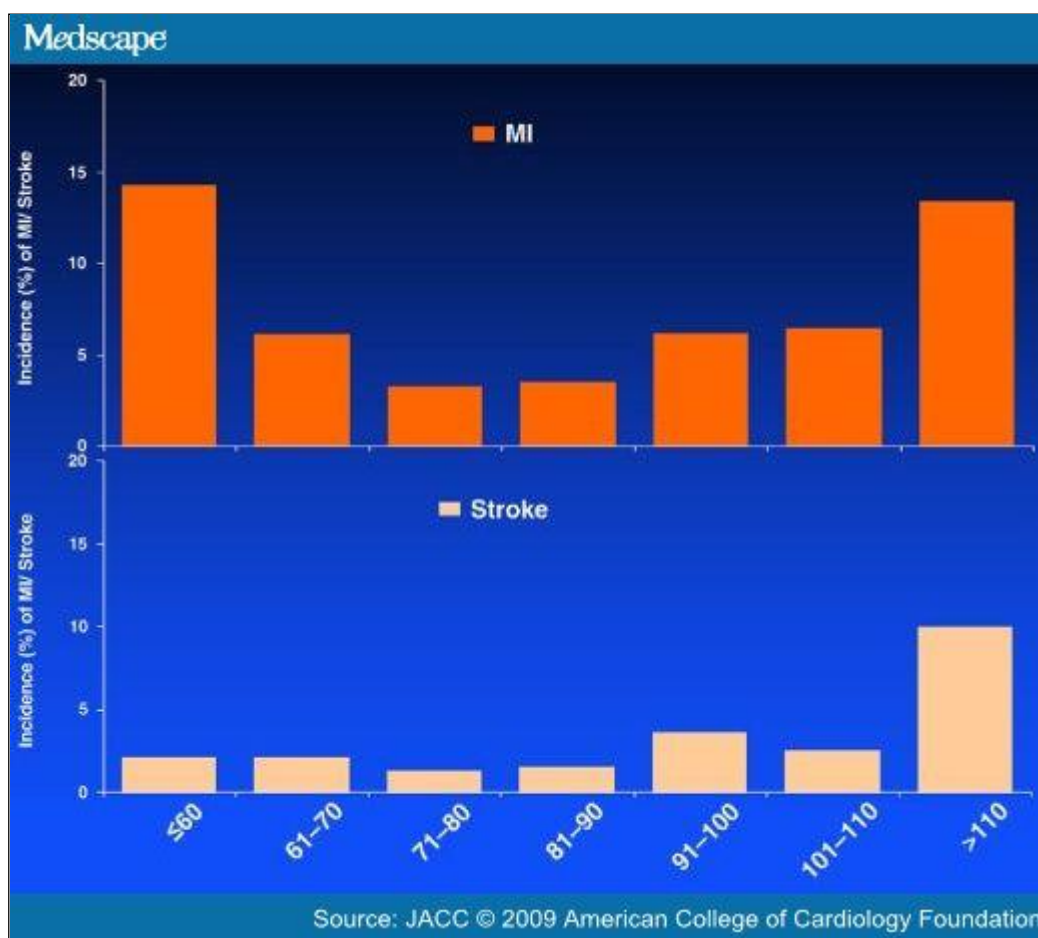
In patients with hypertension and established LVH, rapidly lowering the DBP to levels of between 85 and 90 mm Hg was reported to cause ischemic T-wave changes on the electrocardiogram (ECG) without symptoms of ischemia.<sup>[15]</sup> In the Skaraborg hypertension project, Lindblad et al.<sup>[16]</sup> demonstrated that lowering of DBP in hypertensive men with ischemic/hypertrophic ECGs increased the risk for a first MI. The opposite was true in men with normal ECGs.

Not surprisingly, on simultaneous ECG and ambulatory BP monitoring of patients over a 24-h period, Owens and O'Brien<sup>[17]</sup> reported a temporary relationship between ischemic events and diastolic (rather than systolic) hypotension in 13 of 14 instances. The ST-segment events were significantly associated with preceding hypotensive events. Similarly,

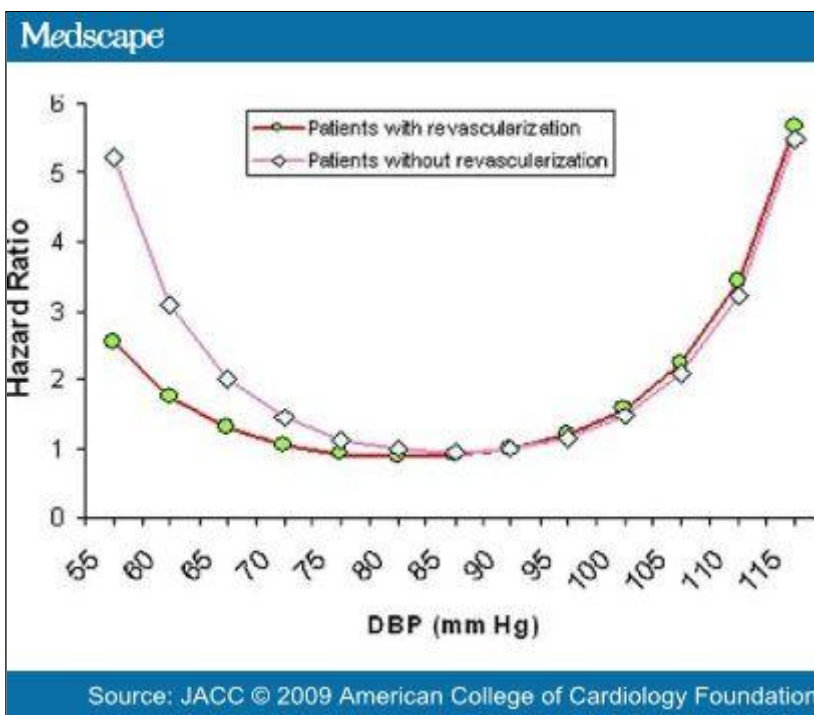
Merlo et al.<sup>[18]</sup> studied 484 elderly men taking antihypertensive medications over a 10-year follow-up and found the risk of an ischemic cardiac event to be higher (more than 2-fold) in men who were taking antihypertensive drugs than in those who were not. In patients with DBP  $\leq 90$  mm Hg the risk of an ischemic cardiac event associated with taking antihypertensive drugs was 4 times higher and remained significantly high after adjustment for other cardiovascular risk factors. These findings support the concept of a J-shaped curve for risk of MI in relation to treated DBP.<sup>[18]</sup>

### Denial of a J-curve

Despite evidence to the contrary in their own studies, some authors have denied the existence of a J-curve. Glynn et al.,<sup>[19]</sup> in the Physician's Health Study and the Women's Health Study, evaluated the risk for MI, stroke, coronary artery bypass, angioplasty, and cardiovascular death associated with both systolic blood pressure (SBP) and DBP in 22,071 men and 39,876 women with a median follow-up duration of 13.0 and 6.2 years, respectively. Investigators claimed an absence of plateau or J-curve in both populations and a lower event rate associated with lower levels of blood. However, upon closer scrutiny, prominent J-curves can be observed in relation to DBP (Figs. 1 and 2 in Glynn et al.<sup>[19]</sup>).



**Figure 1.** Incidence of MI and Stroke Stratified by Diastolic Blood Pressure in the INVEST Study  
 Reproduced with permission from Messerli et al.<sup>[29]</sup> INVEST = International Verapamil-Trandolapril; MI = myocardial infarction.



**Figure 2.** Interaction of the J-Curve With Coronary Revascularization

Patients who were revascularized better tolerate a lower diastolic blood pressure (DBP) than those who were not.

In the HOT (Hypertension Optimal Treatment) study, Hansson et al.<sup>[20]</sup> and Cruickshank<sup>[21]</sup> scrutinized the high-risk patient group with coronary ischemia. He found that there was a 22% increase in the risk of MI when the DBP was <80 mm Hg compared with <85 mm Hg. The relationship between MI and DBP was J-shaped in patients with coronary ischemia but not in nonischemic patients.

In the Cardiovascular Health Study, Psaty et al.<sup>[22]</sup> concluded that "the association between BP level and cardiovascular disease (CVD) risk was generally linear; specifically, there was no evidence of a J-shaped relationship." Yet again, on closer scrutiny, a J-shaped relationship between DBP and MI is observed with a nadir at  $\leq 69$  mm Hg. Additionally, a similar relationship was observed between DBP and risk of death in all 4,902 subjects.

### Mechanism(s) of the J-curve Phenomenon

Three pathophysiologic mechanisms have been proposed to explain the existence of a J-curve: 1) low DBP could be an epiphenomenon to coexisting or underlying poor health or chronic illness leading to increasing morbidity and mortality (reverse causality); 2) low DBP could be caused by an increased pulse pressure reflecting advanced vascular disease and stiffened large arteries; and 3) over-aggressive antihypertensive treatment could lead to too-low DBP and thus hypoperfusion of the coronaries resulting in coronary events.

#### Reverse Causality

Chronic disease states such as neoplasms, chronic infection, malnutrition, and ischemic and nonischemic LV dysfunction can lead to low BP<sup>[23–26]</sup> The National Institute on Aging-sponsored EPESE (Established Populations for Epidemiologic Studies of the Elderly) studied more than 10,000 elderly patients over 5 years to assess the relationship between BP and cause-specific mortality. At 2 years, SBP showed a J-curve relationship with all-cause mortality. All-cause mortality, CVD, and cancer mortality were highest in the low-DBP group (<75 mm Hg). Thus, comorbidities such as cancer and thus low weight and hypotension were the confounding factors that obscured the true relationship of BP and mortality.

A meta-analysis by Boutitie et al.<sup>[27]</sup> on 40,233 hypertensive patients from 7 randomized trials showed a positive J-curve relationship between DBP as well as SBP and both fatal cardiovascular and noncardiovascular mortalities. The authors concluded that the J-curve relationship is possibly attributed to poor health, because it was independent of either treatment or type of events. The NHANES (National Health and Nutrition Examination Survey) showed a J-curve between DBP and cardiovascular mortality in patients older than 55 years, even after correcting for regression dilution bias and removing confounders, such as patients with serious illnesses.<sup>[28]</sup> In contrast, in the INVEST (International Verapamil-Trandolapril) study neither body mass index nor diagnosis of cancer interacted with the J-curve between diastolic pressure and primary

outcome, arguing against weight loss/cachexia or malignancies as being the cause of this observation.<sup>[29]</sup> Thus, although the role of reverse causality in causing a J-curve phenomenon or "epiphenomenon" cannot be ruled out, evidence supporting it as the only or the major contributor is unconvincing.

#### Increase in Pulse Pressure

Increase in pulse pressure has been shown to increase the risk of a coronary event; in fact, an increased pulse wave velocity is a powerful independent predictor of cardiovascular events,<sup>[30]</sup> specifically of coronary heart disease.<sup>[31]</sup> Vaccarino et al.<sup>[32]</sup> found that a 10-mm increase in pulse pressure was associated with a 12% increase in coronary heart disease risk in 2,000 elderly patients followed up for 10 years. A recent subanalysis of the Systolic Hypertension in the Elderly Program revealed that a drug-induced decrease of merely 5 mm Hg in diastolic pressure significantly increased cardiovascular events.<sup>[33]</sup> Benetos et al.,<sup>[34]</sup> in a large French population (n = 77,023), found men with systolic hypertension to be at greater risk when their diastolic pressure was below normal than when they had a mild-to-moderate increase in diastolic pressure. Similarly, Glynn et al.<sup>[35]</sup> found pulse pressure to be the best simple predictor for cardiovascular mortality in a large (n = 9,431) elderly population study organized by the National Institute of Aging.

In the Framingham cohort, in patients free of CVD, Kannel et al.<sup>[36]</sup> found an increase in both crude as well as age- and risk-factor-adjusted rate of CVD at low DBP (<80 mm Hg). However, this increase in the rate of CVD was accompanied by increased SBP. The authors concluded that the excess CVD risk and mortality at low DBP is attributable to individuals with a concomitant increase in SBP (i.e., "an increased pulse pressure"). The CVD risk became substantial at pulse pressures of >45 mm Hg without an increase in nonfatal CVD risk at low pulse pressures. Interestingly, for a fixed systolic pressure, diastolic pressures below 80 mm Hg were associated with increased cardiovascular risk.

Also, in a pooled analysis of individual patient data from 3 large trials involving approximately 8,000 patients, Blacher et al.<sup>[37]</sup> showed that a 10-mm wider pulse pressure increased the risk of major cardiovascular complications. At any level of SBP end points also increased with lower DBP.

The fact that, in several major studies of populations of hypertensive patients, pulse pressure was documented to be an independent risk factor for coronary heart disease irrespective of systolic pressure leads to the conclusion that there has to be an inverse relationship between DBP and coronary heart disease (i.e., the lower the DBP the greater the risk of coronary heart disease). However, 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.

In a reanalysis of the Framingham cohort, Franklin et al.<sup>[31]</sup> showed that the combined evaluation of SBP and DBP conferred superior risk prediction over individual components; strikingly, only DBP showed a nonlinear, quadratic relation with CVD risk. For any given SBP, odds of CVD events increased in a J-curve fashion at extremes of DBP (odds ratio: 2 to 3). As expected, odds of CVD events increased monotonically with increasing SBP at any given DBP.

#### Antihypertensive Therapy and J-curve

As mentioned in the preceding text, 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 nonischemic group.<sup>[20,21]</sup> Thus, the HOT study establishes a J-curve relationship between DBP and the risk of MI in patients with documented coronary heart disease<sup>[20,21]</sup> but not in those without coronary heart disease, a finding akin to that described in the original study of Cruickshank et al.<sup>[7]</sup>

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. 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. In contrast, the nadir for SBP was 119 mm Hg, and the curve between SBP and outcome was much shallower than with DBP. Interestingly enough, in contrast to the risk of acute MI, the risk of stroke did not increase with low DBP (Fig. 1). Also, patients who were revascularized tolerated a lower DBP better than patients who were not revascularized (Fig. 2).

Lubsen et al.,<sup>[38]</sup> who compared hypertensive subjects with normotensive subjects in the ACTION (A Coronary disease Trial Investigating Outcome with Nifedipine GITS) trial, concluded that "our data for normotensive subjects are compatible with the existence of a J-shaped relationship (or more correctly a reverse L-shaped relationship) because in this sub-group there were nonsignificant trends towards higher rates of the primary combined endpoints." More recently Protogerou et al.,<sup>[39]</sup> in an elderly population, again found a J-shaped curve between cardiovascular death and all-cause

death and diastolic strata but not SBP strata. In further analyzing this relationship, the authors concluded that "this association was not a simple epiphenomenon because of concomitant chronic illness, cardiac failure or increased arterial stiffness but was associated with reduced peripheral resistance/pressure wave reflections and potentially aggressive BP reduction, possibly jeopardizing coronary perfusion." Finally, Fagard et al.,<sup>[40]</sup> in a subanalysis of the Syst-Eur (Systolic Hypertension in Europe) study, also showed that low DBP with active treatment was associated with an increased risk of cardiovascular events but only in patients with coronary heart disease at baseline.

Although there is substantial evidence to support an association between antihypertensive therapy and a J-curve phenomenon, a causal relationship has not been established. Similarly, studies with data arguing against the existence of a J-curve have major limitations, such as recording of BP immediately before cardiovascular events or other adverse outcomes. Table 1 and Table 2 list clinical studies where data support<sup>[6,7,16,33,36-55]</sup> or refute<sup>[19-22]</sup> the existence of a J-curve. It is notable that the end point of MI has the most significant association with low DBP, supporting the hypothesis discussed earlier.

Table 1. Summary of Clinical Studies Reporting Association Between Low DBP and Adverse End Points

First Author/Study Name (Ref. #)	Year	Subjects (n)	Mean Age (yrs)	Mean Entry DBP (mm Hg)	Includes Subjects With CVD	Mean Follow-Up (yrs)	J-Curve Relationship for DBP and Event			J-Point DBP (mm Hg)
							MI	Stroke	Total Mortality or Non-CV Events	
Cruickshank <sup>[7]</sup>	1987	902	55	109	Yes	6.1	Yes	No	No	85–90 (in ischemic patients only)
Fletcher <sup>[41]</sup>	1988	2,145	51	107	Yes	4.0	Yes	No	No	86–91
Abernethy <sup>[42]</sup>	1986	10,053	51	90–104	Yes	4.0	—	—	Yes	*26
Waller <sup>[43]</sup>	1988	3,350	50	110	Yes	6.5	Yes	No	No	91–98
Cooper <sup>[44]</sup>	1986	884	68	98	Yes	4.4	Yes	—	—	80–89
Stewart <sup>[6]</sup>	1979	169	44	124	No	6.3	Yes	—	—	100–109
Alderman <sup>[45]</sup>	1989	1,765	51	102	Yes	4.2	Yes	No	—	84–88
Staessen <sup>[46]</sup>	1989	840	71	101	Yes	4.7	Yes	Yes	Yes	90–95
IPPPSH <sup>[47]</sup>	1985	6,357	52	108	No	4.0	Yes	—	—	92
ANBP <sup>[48]</sup>	1981	3,931	50	101	No	4.0	Yes	Yes	—	85–89
Wilhelmsen <sup>[49]</sup>	1987	6,569	40–60	107	No	3.9	Yes	Yes	Yes	86–89
Samuelsson <sup>[50]</sup>	1990	686	52	106	Yes	12.0	Yes	Yes	—	81
McCloskey <sup>[51]</sup>	1992	912	30–79	104	Yes	3–21	Yes	No	—	84
Lindblad <sup>[16]</sup>	1994	2,574	59	92	Yes	7.4	Yes	—	—	90–95
Somes <sup>[33]</sup>	1999	4,736	72	77	Yes	5.0	Yes	Yes	—	60–65
Hasebe <sup>[52]</sup>	2002	234	64	88	Yes	6.0	Yes	—	—	95–104
Pastor-Barruso <sup>[53]</sup>	2003	7,830	54	82	No	15.0	Yes	Yes	—	80
Zanchetti <sup>[54]</sup>	2003	18,790	62	100–115	No	3.8	Yes	No	Yes (in smokers only)	80–85

Pepine <sup>[55]</sup>	2003	22,576	66	86	Yes	2.7	Yes	Yes	Yes	76.4–85.8
Kannel <sup>[36]</sup>	2004	7,798	35–80	—	No	10.0	Yes	Yes	No	80–89
Lubsen <sup>[38]</sup>	2005	7,661	63	80	Yes	4.9	Yes	Yes	Yes	—
Protegoru <sup>[39]</sup>	2007	331	85	—	Yes	3–4	Yes	Yes	Yes	<70
Fagard <sup>[40]</sup>	2007	4,695	70	85	Yes	1–8	Yes	Yes	Yes	*70–75

Summary of clinical studies in patients receiving antihypertensive medications and evidence of

J-curve phenomenon. \*In patients with coronary artery disease

ANBP = Australian National BP Study; CV = cardiovascular; CVD = cardiovascular disease; DBP = diastolic blood pressure; IPPPSH = International Prospective Primary Prevention Study in Hypertension; MI = myocardial infarction.

Table 2. Summary of Clinical Studies Reporting No Clear Association Between Low DBP and Adverse End Points But Upon Further Inspection of Data Pointing to Existence of a J-Curve

First Author/Study Name (Ref. #)	Year	Subjects (n)	Mean Age (yrs)	Mean Entry DBP (mm Hg)	Include Subjects With CAD	Mean Follow-Up (yrs)	MI	Stroke	Total Mortality or Non-CV Events	J-Point DBP (mm Hg)
Hansson <sup>[20]</sup>	1998	18,790	62.0	105.0	Yes	3.8	Yes	No	No	80–85*
Psaty <sup>[22]</sup>	2001	4,902	72.6	71.0	No	6.7	Yes	No	No	≤69
Glynn/PHS <sup>[19]</sup>	2002	22,071	53.2	78.8	No	13.0	Yes	No	No	65–70
Glynn/WHS <sup>[19]</sup>	2002	39,876	53.8	77.7	No	6.2	Yes	No	No	70

\*In patients with ischemia.

PHS = Physician's Health Study; WHS = Women's Health Study.

Finally, in a recent commentary on importance of SBP as a target, Williams et al.<sup>[56]</sup> have invoked the argument that "trials have not shown that a resultant fall in DBP would impart harm or off set the benefit of SBP reduction." Although we agree that SBP reduction should be the goal, caution has to be exercised in lowering the diastolic component beyond a critical "J-point." This might be even more important in elderly patients where DBP might already be reduced due to age at onset of therapy.

### Antihypertensive Therapy and Safety Zone of DBP

The interaction of antihypertensive drugs on BP and coronary hemodynamic status is complex, and head-to-head comparisons among drugs or drug classes are lacking. However, at least 3 different pathophysiologic mechanisms deserve consideration. First, although all antihypertensive drugs lower BP, they do not have quantitatively similar effects on pulse pressure. Most drug classes, such as blockers of the renin angiotensin system and calcium antagonists as well as the diuretics, improve arterial compliance and thus lower SBP more than DBP and therefore diminish pulse pressure. In contrast beta-blockers, because they decrease heart rate, increase stroke volume and have a less favorable effect on pulse pressure than the other drug classes; beta-blockers (with the notable exception of vasodilating agents such as carvedilol and nebivolol) also have been shown to exert a pseudo-antihypertensive effect in that they lower peripheral BP more than central pressure. Second, drug classes that decrease heart rate allow for more prolonged diastolic perfusion of the coronary vascular bed. By this mechanism, heart rate-lowering drugs, such as beta-blockers and some calcium antagonists (verapamil, diltiazem), have an advantage over those that do not affect heart rate. In contrast, antihypertensive drug classes that accelerate heart rate might have a detrimental effect on coronary perfusion. Indeed, short-acting calcium antagonists and other arteriolar vasodilators (i.e., hydralazine, minoxidil) are prone to cause myocardial ischemia in susceptible patients.<sup>[4]</sup> Third, antihypertensive drug classes that reduce LVH and hypertensive vascular disease are more effective over the long term in improving coronary flow reserve than drug classes that have little or no effect. Thus, blockers of the renin angiotensin system, calcium antagonists as well as the diuretics, have been shown to reduce LV

hypertension<sup>[57]</sup> and hypertensive vascular disease<sup>[58–60]</sup> and improve arterial compliance<sup>[61]</sup> better than beta-blockers. Drugs that improve arterial compliance slow the reflected wave so it might supplement coronary filling during diastole rather than arrive during systole and increase cardiac workload.

## Conclusions

Numerous studies have documented 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. At the same reduced DBP levels, there is little if any evidence of a J-shaped curve with regard to other target organs, such as the brain and the kidney. Moreover, few if any J-shaped curve phenomena have been documented between systolic pressure and coronary, renal, or cerebrovascular events. However, careful scrutiny of the available data seems to show a J-shaped relationship between DBP and coronary heart disease in high-risk patients. These are often characterized by being elderly, having LVH and/or coronary heart disease, and by exhibiting a wide pulse pressure.

Thus, there might be more than just a semantic reason for hypertension to remain "essential"; this seems to be particularly true for DBP in patients with CAD. Unfortunately, the arguments surrounding the J-curve phenomenon have often become unnecessarily contentious. However, these considerations 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 BPs of <140/90 mm Hg.<sup>[62]</sup>

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**Abbreviations and Acronyms**

BP, blood pressure; CAD, coronary artery disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; ECG, electrocardiogram; LV, left ventricle/ventricular; LVH, left ventricular hypertrophy; MI, myocardial infarction; SBP, systolic blood pressure

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