JACC Vol. 20, No. 4
October 1992:1003–4



*Editorial Comment*

# Blood Pressure Reduction and Recovery of Stunned Myocardium in the Hypertrophied Hypertensive Heart*

JOSEPH A. DIAMOND, MD,
ROBERT A. PHILLIPS, MD, PHD, FACC
*New York, New York*

**Effect of blood pressure reduction on patients with coronary artery disease.** Lowering high blood pressure in arterial hypertension significantly decreases the incidence of nonfatal and fatal strokes (1), but the reduction in death from coronary artery disease has not been as pronounced. Analysis of several large prospective observational studies (2) suggests that a 5- to 6-mm Hg decrease in diastolic blood pressure would cause a 20% to 25% reduction in coronary events. However, this degree of reduction in blood pressure has resulted in only a 14% decrease in coronary events (3).

One controversial explanation for this discrepancy is that a J curve describes the relation between mortality rate from myocardial infarction and treated diastolic blood pressure (4). Support for and against this relation is based on differing interpretations of retrospective analyses of several large treatment trials or programs (5–9). The J curve implies that hypertensive subjects without coronary disease may benefit from decreasing blood pressure as much as possible, but those with ischemic disease with a treated diastolic blood pressure of <85 mm Hg may have an upturn in coronary events, presumably as a result of inadequate perfusion of stenosed coronary arteries.

Because of altered coronary flow reserve and coronary autoregulation, hypertensive subjects with left ventricular hypertrophy may be another group at risk for adverse events with excessive lowering of blood pressure. The increase in myocardial blood flow with maximal coronary vasodilator stress is blunted in hypertrophy and theoretically this deficit may be exacerbated at lower perfusion pressures (10). In addition, the range of coronary perfusion for which coronary flow is kept constant is shifted to the right and higher in patients with hypertrophy. As a result, loss of autoregulation occurs at relatively higher coronary perfusion pressures. Thus, a recent study in patients (11) demonstrated that hypertensive subjects without left ventricular hypertrophy maintain constant coronary flow as perfusion pressure is markedly reduced with nitroprusside from 120 to 70 mm Hg, but patients with hypertension and hypertrophy have a large decrease in flow as pressure is reduced from 90 to 70 mm Hg. Nevertheless, experimental data (12,13) have clearly demonstrated that myocardial infarction will be limited in the hypertrophied heart if blood pressure is decreased toward normal, either before or during prolonged coronary occlusion. These studies (12,13), however, did not address the issue of the effect of blood pressure reduction on recovery after myocardial stunning due to a transient ischemic insult.

**The present study.** In this issue of the Journal, Taylor et al. (14) explore a novel model that may become increasingly important in the thrombolytic era: the effect of blood pressure reduction on recovery of blood flow and systolic function in the stunned, hypertrophied myocardium. Three groups of chronically instrumented conscious dogs were tested. In two groups, hypertension and left ventricular hypertrophy were induced by creating renal artery stenosis and removing the contralateral kidney (one-kidney, one-clip hypertension). In one of these groups, after left ventricular hypertrophy was induced, blood pressure was returned toward normal by release of the renal artery clamp. The third group consisted of normotensive control dogs without hypertrophy. After 15 min of ischemia all groups underwent reperfusion for 24 h. Segmental systolic thickening and regional myocardial blood flow were measured serially.

Contrary to the authors' hypothesis, hypertensive dogs with hypertrophy recovered systolic function as quickly as did control dogs. In contrast, dogs with hypertrophy and reduced arterial blood pressure had a significant decrease in recovery of systolic thickening from immediate reflow to 120 min of reperfusion but with return to control function by 24 h of reflow. Furthermore, the group with hypertrophy and reduced blood pressure was the only one in which regional blood flow to hypokinetic segments did not return to its preocclusion baseline level after 30 min of reperfusion. Similar observations were made in an experimental infarct model (13) in which, after release of coronary occlusion, blood flow tended to improve more quickly in dogs that remained hypertensive than in dogs whose blood pressure was deliberately decreased. Although recovery of blood flow may be irrelevant in an infarct zone, the rate of its recovery in ischemic or stunned myocardium may be of critical importance, because these cells are still viable. One must be careful, however, in assuming that decreased myocardial perfusion accounts for the slower recovery of systolic function in the stunned myocardium, because in the Taylor study (14), coronary blood flow during reperfusion was only measured once, at 30 min.

**Implications.** These results may fuel the controversy on the optimal degree of reduction in blood pressure and the

*Editorials published in *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of JACC or the American College of Cardiology.

From the Hypertension Section, Division of Cardiology, Mount Sinai School of Medicine, New York, New York.

Address for correspondence: Robert A. Phillips, MD, PhD, Hypertension Section, Division of Cardiology, Box 1085, Mount Sinai Medical Center, One Gustave L. Levy Place, New York, New York 10029.



0735-1097/92/$5.00

JACC Vol. 20, No. 4
October 1992:1003–4

most appropriate agents to use. The current study (14) suggests that in hypertensive subjects with hypertrophy who experience an ischemic event that may be associated with myocardial stunning (angina, unstable angina, coronary occlusion with early reperfusion), recovery of both blood flow and systolic function may be impaired if blood pressure is lowered below a critical point. In a similarly designed study it would be interesting to determine the effect of various degrees of blood pressure reduction on recovery of systolic function and blood flow. Furthermore, calcium channel blocking agents hasten recovery of stunned, nonhypertrophied myocardium (15–17), and it would be useful to know the effect of these drugs and other classes of antihypertensive agents on the stunned hypertrophied heart. It is likely that differences will emerge (17,18). Such information might then provide a better rationale than is currently available (19) for choice of pharmacologic therapy of the hypertensive subject with left ventricular hypertrophy, as well as better understanding of the degree to which blood pressure can be safely decreased.

## References

1. Veterans Administration Cooperative Study Group on Antihypertensive Agents. Effects of treatment on morbidity in hypertension: results in patients with diastolic blood pressures averaging 115 through 129 mm Hg. JAMA 1967;202:1028–34.
2. MacMahon S, Peto R, Cutler J, et al. Blood pressure, stroke, and coronary heart disease Part 1. Prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. Lancet 1990;335:765–74.
3. Collins R, Peto R, MacMahon S, et al. Blood pressure, stroke, and coronary heart disease. Part 2. Short-term reductions in blood pressure: overview of randomized drug trials in their epidemiological context. Lancet 1990;335:827–38.
4. Cruickshank JM, Thorp JM, Zacharias FJ. Benefits and potential harm of lowering high blood pressure. Lancet 1987;1:581–4.
5. Alderman MH, Ooi WL, Madhavan S, Cohen H. Treatment-induced blood pressure reduction and the risk of myocardial infarction. JAMA 1989;262:920–4.
6. Farnett L, Mulrow CD, Linn WD, Lucey CR, Tuley MR. The J-curve phenomenon and the treatment of hypertension. Is there a point beyond which pressure reduction is dangerous? JAMA 1991;265:489–95.
7. Fletcher AE, Bulpitt CJ. How far should blood pressure be lowered? N Engl J Med 1992;326:251–4.
8. McCloskey LW, Psaty BM, Koepsell TD, Aagaard GN. Level of blood pressure and risk of myocardial infarction among treated hypertensive patients. Arch Intern Med 1992;152:513–20.
9. Weinberger MH. Do no harm. Antihypertensive therapy and the "J" curve. Arch Intern Med 1992;152:473–6.
10. Hoffman JI. A critical view of coronary reserve. Circulation 1987; 75(suppl II):I-6–11.
11. Polese A, DeCesare N, Montorsi P, et al. Upward shift of the lower range of coronary flow autoregulation in hypertensive patients with hypertrophy of the left ventricle. Circulation 1991;83:845–53.
12. Inou T, Lamberth WC, Koyanagi S, Harrison DG, Eastham CL, Marcus ML. Relative importance of hypertension in infarct size and the incidence of sudden death after coronary occlusion in chronic hypertensive dogs with left ventricular hypertrophy. Am J Physiol 1987;22:1148–58.
13. Dellsperger KC, Clothier JL, Hartnett JA, Haun LM, Marcus ML. Acceleration of the wavefront of myocardial necrosis by chronic hypertension and left ventricular hypertrophy in dogs. Circ Res 1988;63:87–96.
14. Taylor AL, Murphree S, Buja LM, Villarreal MC, Pastor P, Eckels R. Segmental systolic responses to brief ischemia and reperfusion in the hypertrophied canine left ventricle. J Am Coll Cardiol 1992;20:994–1002.
15. Przyklenk K, Kloner RA. Effect of verapamil on postischemic "stunned" myocardium: importance of the timing of treatment. J Am Coll Cardiol 1988;11:614–23.
16. Przyklenk K, Ghafari GB, Eitzman DT, Kloner RA. Nifedipine administered after reperfusion ablates systolic contractile dysfunction of postischemic "stunned" myocardium. J Am Coll Cardiol 1989;13:1176–83.
17. Taylor AL, Gollino P, Eckels R, Pastor P, Buja M, Willerson JT. Differential enhancement of postischemic segmental systolic thickening by diltiazem. J Am Coll Cardiol 1990;15:737–47.
18. Przyklenk K, Kloner RA. Is "stunned myocardium" a protective mechanism? Effect of acute recruitment and acute beta-blockade on recovery of contractile function and high-energy phosphate stores at 1 day postreperfusion. Am Heart J 1989;118:480–9.
19. Dahlof B, Pennert K, Hansson L. Reversal of left ventricular hypertrophy in hypertensive patients: a metaanalysis of 109 treatment studies. Am J Hypertens 1992;5:95–110.