



Hypertension and Myocardial Infarction

FRANCIS G. DUNN, MB, ChB, FACC

New Orleans, Louisiana

Because hypertension and myocardial infarction are closely linked in several ways, a better understanding of this relation leads to more effective prophylaxis and management. Management should be directed at three different areas: 1) the prevention of a first myocardial infarction, 2) the prevention of complications after an infarction, and 3) the management of hypertension dur-

ing evolution of an acute infarction. There is good evidence that beta-receptor blocking agents are beneficial to long-term management. When therapy is required in the acute situation, arteriolar vasodilators are to be avoided and combined arteriolar/venular dilators are the drugs of choice.

An appreciation of the association between myocardial infarction and hypertension extends back for at least 40 years. In 1940, Sir Thomas Lewis wrote, "Thrombosis of a coronary vessel is an accident occurring chiefly in men in their fifties or sixties: it happens occasionally in women; it is rare before the age of forty. The subjects usually present signs of arterial disease and more often as not high blood pressure" (1). More recently, evidence has confirmed that this association is not simply one of risk factor and disease because pathophysiologic and hemodynamic factors also participate. This article focuses on the different ways in which hypertension and myocardial infarction are linked (Fig. 1) and on management of systemic hypertension in the context of an acute or a previous myocardial infarction.

The Link Between Hypertension and Myocardial Infarction

Risk factor. Both systolic and diastolic hypertension increase the risk of a myocardial infarction (2,3) and the higher the pressure, the greater the risk (2). Even when other major risk factors are absent, the increased risk still exists (2,3). Almost 40% of patients with ischemic heart disease who die suddenly have a history of hypertension (4). The immediate and long-term mortality after infarction in patients with hypertension is increased. This is likely to be due at least in part to the frequency of complications such as cardiac rupture and ventricular septal defect (5).

The potency of hypertension as a risk factor is not uniform throughout the world. For example, the black people in southern Africa, despite a similar incidence of hypertension and hypertensive heart disease, have a very small incidence of myocardial infarction, presumably in part because of a low serum cholesterol level (6).

Because blood pressure is frequently altered after acute myocardial infarction, the patient's risk status is immediately altered. Kannel et al. (7) provided important information on this subject. Thus, myocardial infarction in men is accompanied by an average sustained decrease in systolic pressure of 10.1 mm Hg. Of patients who were hypertensive before the myocardial infarction, 40% had normalization of pressure and 18% manifested a reversion from sustained to borderline hypertension. The higher the initial pressure, the more likely it was to decrease; those who experienced a decrease were at a greater risk of heart failure. When patients with decreases of 10 mm Hg were excluded, blood pressure status after infarction continued to be related to mortality. In view of these findings, it is clear that a reappraisal of the individual patient's hypertensive status is needed after an acute myocardial infarction. Therapy is indicated for those who remain hypertensive, and the same goals should be set for this group as for other patients with hypertension.

Atherogenic factor. The term "myocardial infarction" signifies a pathologic entity and says nothing of the mechanisms producing the infarct (although a previous commonly used term "coronary thrombosis" implied both mechanism and pathologic entity). There are, of course, several ways in which myocardial necrosis can occur, including coronary artery spasm, coronary embolism, coronary artery dissection and a variety of different myocardial toxins. Nonetheless, by far the most common cause is atherosclerotic coronary artery disease, and whether the precipitating event is throm-

From the Division of Hypertensive Diseases, Ochsner Clinic and Alton Ochsner Medical Foundation, New Orleans, Louisiana.

Address for reprints: Francis G. Dunn, MD, Ochsner Clinic, 1514 Jefferson Highway, New Orleans, Louisiana 70121.

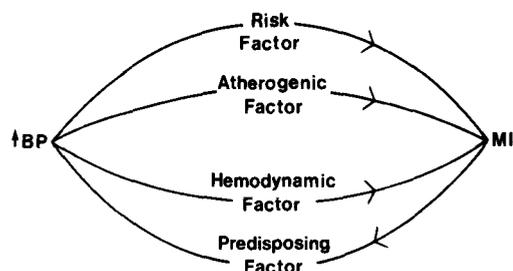


Figure 1. The links between hypertension and myocardial infarction (MI).
↑ BP = elevated blood pressure

bosis, spasm or plaque rupture, atheroma is the pathologic hallmark in most cases of myocardial infarction.

There is good evidence from different sources pointing to the role of hypertension in accelerating if not initiating atherosclerosis. A greater percent of the intimal surface of the aorta, coronary artery and cerebral artery is affected by raised lesions in hypertensive persons than in normotensive persons (8). The prevalence of coronary occlusive lesions is also more common in patients with hypertension (8). Pulmonary artery atherosclerosis is extremely rare except in the presence of pulmonary hypertension (9). Many years ago, Burch and dePasquale (10) reported a fascinating case in which an anomalous left coronary artery (arising from the pulmonary circulation) had virtually no atheroma, whereas the normally arising right coronary artery showed much more atherosclerotic change. An autopsy analysis of children with nephrotic syndrome and hypercholesterolemia has demonstrated coronary artery changes only in those children also having an elevated blood pressure (11).

Studies in both animals and human beings have emphasized the importance of cholesterol in hypertension-accelerated atherosclerosis, and it appears that in the presence of a low cholesterol level, the atherosclerotic potential of hypertension is lessened (6). In addition to the mechanical stress on the vessels, vasoactive substances may play a role in the development of atherosclerosis. Norepinephrine has been reported to produce atherosclerosis in rabbits (12), and angiotensin (13) and prostaglandin (14) have been known to increase vascular permeability. However, the role of vasoactive substances remains conjectural at the present time.

Hemodynamic factors and effects on left ventricular function. It is now well established that the hemodynamic characteristics of essential hypertension are not homogeneous. Thus, early in the development of hypertensive vascular disease, cardiac output may be elevated (15). However, with advancing vascular disease, progressively increasing total peripheral resistance and developing left ventricular hypertrophy, cardiac output will start to decrease and left ventricular function will deteriorate (15,16). In addition, both hypertension and left ventricular hypertrophy have important effects on myocardial perfusion. Systolic

intraventricular pressure is a key determinant of myocardial oxygen consumption (17) and therefore myocardial oxygen demand will progressively increase as systolic pressure increases. Furthermore, left ventricular hypertrophy is known to be associated with a variety of factors that could adversely affect the response to coronary occlusion. These include a decrease in capillary density (18), a failure of vasodilator capacity to increase in parallel with muscle mass (19), an increase in coronary collateral resistance (20), more severe subendocardial involvement and larger ischemic zones (20). Thus, myocardial perfusion and ventricular function abnormalities occur in hypertension, independent of those abnormalities known to occur in ischemic heart disease.

Hypertension occurring during myocardial infarction. There is sound evidence that hypertension can occur de novo in the evolution of a myocardial infarction (21,22). This can take the form of combined systolic and diastolic hypertension (21) or isolated systolic hypertension (23). The reported incidence rate varies considerably from less than 5% to 43% (21,23). No specific relation appears to exist between the location of the infarct and the presence of hypertension, but there does appear to be a relation to the frequency of proximal left main stem coronary artery disease (21). Several mechanisms have been suggested. The anxiety caused by the pain could raise the blood pressure, although it has been shown that elevation of blood pressure may precede cardiac pain (24). High levels of circulating catecholamines are a possible explanation and there is evidence to support this (25). Another interesting postulate is that the hypertension is caused through activation of a cardiogenic reflex initiated perhaps by the release of serotonin from platelet aggregation in the proximal left coronary circulation (21). However, the exact mechanism of the increase in blood pressure remains to be clarified.

Clinical Evaluation

A full discourse on the clinical assessment of the patient with hypertension and myocardial infarction will not be presented. However, several points merit emphasis. Because atherosclerotic changes in the coronary arteries increase the likelihood of atheroma elsewhere, careful exclusion of renal artery stenosis is indicated, particularly when the hypertension is of recent onset. Hypokalemia, whether due to diuretic therapy or to a primary adrenal disorder, should be investigated and treated vigorously in view of the danger of ventricular premature complexes, which may be already increased as a result of ischemic heart disease. Pheochromocytoma may be heralded by a malignant ventricular arrhythmia, by myocardial infarction or even by sudden death (26). In all patients who present with myocardial infarction and hypertension, the diagnosis of pheochromocytoma should be kept in mind and a particularly assiduous search should be made for this entity in younger patients.

Diagnosis. Because diagnosing acute myocardial infarction in patients with hypertension on electrocardiographic grounds may be difficult because of the presence of preexisting ST and T wave changes, greater reliance has to be placed on the history, cardiac enzymes and rest myocardial perfusion scans. Conversely, if a previous myocardial infarction has altered electrical forces, this may greatly reduce the ability of the electrocardiogram to aid in diagnosis of left ventricular hypertrophy. A two-dimensional echocardiogram will be needed to confirm the presence of left ventricular hypertrophy. This modality is preferable to the M-mode echogram which has known limitations in patients with the segmental wall motion abnormalities seen in coronary artery disease.

Management

Role of antihypertensive treatment in incidence of myocardial infarction. Is treatment of hypertension effective in reducing the incidence of myocardial infarction? Confusion in the published reports regarding this question is understandable (Table 1) when one considers that hypertension is only one of many factors that predispose a patient to infarction. Furthermore, clinical trials use clinical end points for obvious reasons, and to date we have no acceptable method of assessing whether risk factor modification affects the atherosclerotic process itself. The composition of the study population also influences results, and even two symptom-free populations without clinical features of ischemic heart disease may have widely varying degrees of atherosclerosis. These points must be considered by those interpreting the results of currently available trials.

Early prospective trials (27,28) did not reveal any significant reduction in myocardial infarction in patients with moderate and severe hypertension, although one retrospective analysis (29) did suggest a possible reduction in clinical events. Berglund et al. (30) followed up a group of 1,026 hypertensive patients and found that those receiving beta-receptor blocking agents showed a definite reduction in the incidence of nonfatal infarction and death. It is possible that

the beta-receptor blocking agents produced a specific protective effect, and later studies on the role of these drugs in myocardial infarction support this hypothesis. However, the study of Berglund et al. was retrospective and was not designed to answer the question at issue.

Of the three major trials reported in the past 2½ years, only the Hypertension Detection and Follow-Up Program Cooperative Group study (31) showed a reduction in myocardial infarction with good blood pressure control (and without beta-receptor blocking agents). Neither the Australian (32) nor the Norwegian (33) study, each placebo-controlled, confirmed this benefit. In fact, the Norwegian study showed a slight (nonsignificant) increase in the incidence of myocardial infarction in the treatment group (Table 1).

What conclusions can be drawn from these studies? It may be presumptuous to expect that modification of one risk factor over a relatively short period of time (in comparison with the duration of development of atherosclerosis) will produce clear-cut results. The approach to reducing myocardial infarction in a community must of its nature be on a multiple risk factor intervention basis. This should include nonpharmacologic and, if necessary, pharmacologic control of blood pressure. Because it is conceivable that patients in the high risk group for myocardial infarction are particularly sensitive to the biochemical adverse effects of diuretic drugs (particularly hypokalemia), beta-receptor blocking agents seem to be a more logical choice of step 1 therapy (Fig. 2). The results of three recent postmyocardial infarction trials have confirmed the benefit of beta-receptor blocking agents in this context after both short-term (34) and long-term (35,36) use. Although the calcium slow channel blocking agents (three of which have been recently introduced in this country for the treatment of angina) offer great potential in patients after a myocardial infarction, their prophylactic value remains to be proved.

Hypertension and infarct size. There has been much interest in recent years concerning the relation between myocardial infarct size and oxygen requirements in acute myocardial infarction (37). We know that reduction in myocardial oxygen requirements can reduce the extent of myocardial injury after coronary occlusion. Because systolic pressure is a major determinant of myocardial oxygen consumption and diastolic pressure has a critical relation to coronary flow, it is clear that both hypertension and hypotension will induce important and possibly adverse hemodynamic effects in acute myocardial infarction. In experimental studies in dogs, the extent of the myocardial damage was dependent on arterial pressure; hypertension reduced myocardial injury and hypotension increased myocardial injury (38). However, it has been shown that reducing blood pressure in human subjects with acute myocardial infarction and hypertension improved hemodynamics and decreased infarct size (39). These discrepant results can be explained by differences in collateral circulation between dogs and

Table 1. Blood Pressure Control and Subsequent Myocardial Infarction: Prospective Trials

	No. of Myocardial Infarctions	
	Placebo/Referred Care	Optimal Therapy
VA trial (27)	2	0
VA trial (28)	3	2
HDFP study (31)	56	30
Australian trial (32)	25	20
Norwegian trial (33)	8	8

HDFP = Hypertension Detection and Follow-up Program; VA = Veterans Administration

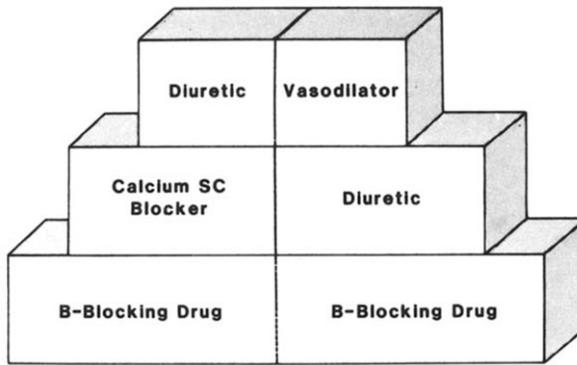


Figure 2. Alternative stepwise approaches to treatment of hypertension in the patient after acute myocardial infarction. The regimen on the **left** may be considered in patients with continuing symptoms of myocardial ischemia. The regimen on the **right** may be considered when hypertension persists. (These regimens are in addition to the use of nitrates.) B = beta; SC = slow channel.

human beings. In the dog, collateral blood supply is highly developed so that the deleterious effects of hypertension on myocardial oxygen consumption are offset by increases in collateral flow to ischemic areas. Patients do not have such extensive collateral circulation and therefore the deleterious effects of hypertension on increasing oxygen consumption are not offset by increases in collateral flow to the ischemic zones. Of course, there is wide individual variation among patients in collateralization and in the optimal blood pressure for adequate cardiac function. It is clear that no precise optimal pressure level can be given. Nonetheless, certain guidelines can assist in determining the approximate pressure that would be most beneficial to the patient with an acute myocardial infarction.

Guidelines for blood pressure reduction in acute myocardial infarction. In most patients, acute hypertension that occurs de novo in the evolution of an acute myocardial infarction will resolve spontaneously within a period of hours. Some workers (23) suggest that a systolic pressure of less than 170 mm Hg should be treated; others (40) argue that the acute increase in systolic pressure is transient and rarely severe and may be supportive in terms of cerebral and renal perfusion. Still others (21) have advocated that no treatment be administered unless the pressure elevation is "severe" or sustained beyond 24 hours. The temporary elevation does not appear to have an adverse effect on the prognosis of acute myocardial infarction. The following is my approach to this difficult clinical problem.

Once the presence of persistent hypertension has been established after pain is relieved, the patient's clinical and hemodynamic status should be assessed. If there is evidence of heart failure, appropriate therapy should be initiated to reduce vascular resistance and ventricular filling pressure (to approximately 15 mm Hg). Pure arteriolar dilators such as hydralazine, minoxidil and diazoxide should not be used because they reflexively increase heart rate and myocardial

contractility (and, therefore, myocardial oxygen consumption and the ischemic area around the infarct) (Table 2). Because nitroprusside and nitroglycerin, by virtue of their venodilating properties, cause only minimal reflexive effects, they are the agents of choice in such circumstances.

If the patient does not have heart failure, a less aggressive approach can be taken; control of arterial pressure should be individualized. Marked elevations of pressure should be treated with nitroprusside or nitroglycerin, whereas less severe pressure elevations can be monitored closely and treated as warranted by the patient's clinical condition. This approach seems to be indicated until we know the optimal perfusion pressure in the first stage of infarction and until we assess the effect of treating moderate hypertension on infarct size.

Oral antihypertensive agents should be used with caution in the immediate postinfarction state because sudden reversal of a drug's hypotensive action may be needed and this may not be easily accomplished with oral therapy. The importance of careful hemodynamic monitoring and titration of therapy cannot be overemphasized when reducing blood pressure after an acute myocardial infarction.

Conclusion

Hypertension is linked to myocardial infarction as a risk factor, an atherogenic factor and a hemodynamic factor. It may also occur in the course of an acute myocardial infarction. Both these disorders have serious adverse cardiac effects and both have profound effects on morbidity and mortality. Although there have been conflicting results regarding reduction in the incidence of myocardial infarction after treatment of hypertension, it is likely that future long-term trends will show a reduced incidence with prolonged control of blood pressure.

Treatment of hypertension in the context of an acute myocardial infarction is a problematic area. Severe hypertension and hypertension in the context of heart failure should be treated with careful hemodynamic monitoring and an appropriate choice of therapy. The development of cardiovascular drugs that are efficacious in both hypertension and myocardial infarction represents a major advance in treat-

Table 2. Cardiac Effects of Parenteral Antihypertensive Agents

	Heart Rate	Cardiac Output	Myocardial Contractility	Myocardial Ischemia
Nitroglycerin	↑	↑	—	—
Nitroprusside	↑	↑	—	—
Diazoxide	↑↑↑	↑↑↑	↑↑↑	↑↑
Minoxidil	↑↑↑	↑↑↑	↑↑↑	↑↑
Hydralazine	↑↑	↑↑	↑↑	↑

↑ = slightly increased; ↑↑ = moderately increased; ↑↑↑ = greatly increased; — = unchanged.

ment when these two disorders coexist and is likely to be reflected in a reduced incidence of initial myocardial infarction and an improved prognosis after its occurrence.

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