The Influence of Impedance on Left Ventricular Performance

THE ROLE OF THE arterial system in determining the performance of the diseased left ventricle has been relatively neglected in traditional thinking about heart failure. Attention has instead been focused on the influence of diastolic filling of the ventricle and of its contractile state. Therapy directed at altering these latter factors in cardiac performance has served as the cornerstone of the management of congestive heart failure. However, recent studies have demonstrated dramatic hemodynamic improvement during administration of vasodilator drugs in patients with left ventricular failure due to acute myocardial infarction, chronic ischemic heart disease, and cardiomyopathy. An understanding of this response requires consideration of the concept of impedance to left ventricular outflow.

During ventricular systole the rise in aortic pressure is related to the stroke volume, its rate of ejection, and the impedance the blood faces as it crosses the aortic valve. Changes in total impedance during ejection are due to alterations in either the compliant component, which opposes a change in volume of the arterial vascular bed, or the resistive component, which opposes runoff of blood from the arterial tree and is determined primarily by the cross-sectional area of the arterioles and the viscosity of blood. If impedance increases because of arteriolar vasoconstriction or reduced arterial compliance, then aortic systolic pressure will rise more rapidly with any given ejection rate, and mean left ventricular systolic pressure will be increased for any given stroke volume. During ejection the rise in left ventricular pressure is accompanied by a reduction in left ventricular chamber size so that wall tension (pressure × radius) normally tends to fall during systole. When impedance is increased, a greater rise in pressure for any given reduction in chamber size means that left ventricular wall tension during systole will be higher. Since wall tension is an important determinant of myocardial oxygen consumption, the greater the impedance the higher the ratio between oxygen cost and stroke volume. This ratio is further increased when the ventricle is dilated, since under these circumstances radius is reduced less during systole for any stroke volume.

An increased impedance to left ventricular ejection will not necessarily alter stroke volume when the heart is normal. Despite an increment in systolic ventricular wall tension (afterload), normal fiber shortening is accomplished primarily by an unexplained compensatory increase in myocardial contractility referred to by Sarnoff as homeometric autoregulation. When left ventricular function is impaired, however, increases in impedance are not tolerated with such impunity. The reserve capacity of the diseased ventricle is limited, and the increased afterload precipitates a reduction of fiber shortening and ejection fraction. A rise in left ventricular end-diastolic pressure may reflect a compensatory increase in end-diastolic fiber length (Frank-Starling mechanism), which tends to support stroke volume. This abnormal increase in ventricular filling pressure serves as the basis for angiotensin infusion and isometric hand grip as tests of subclinical ventricular dysfunction. The abnormal ventricle faced with heightened impedance therefore exhibits an increased ventricular volume and pressure with a reduced ejection fraction resulting in the consumption of more oxygen to deliver a smaller stroke volume.

A high impedance during left ventricular outflow is characteristic of clinical heart failure. Arteriolar vasoconstriction may result from reflex activation of the sympathetic nervous system or the release of renin or other humoral vasoconstrictor substances. An increase in sodium and water content of vessel walls and an increase in interstitial volume and pressure also may reduce cross-sectional area of the vascular bed and increase both the resistive and

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compliant components of impedance. In addition, a reduction of flow velocity in the microcirculation increases the viscosity of blood and may contribute to a further rise in resistive impedance. When the heart is normal and stroke volume falls because of a primary reduction in venous return, an increase in peripheral resistance serves as an appropriate compensatory mechanism by which aortic pressure is supported. However, when stroke volume falls because of cardiac impairment, a rise in resistance may be detrimental. The cerebral and coronary circulations may be protected from the lethal effects of hypotension, but the increase in impedance may further decompensate the failing left ventricle. Unfortunately, the impedance is not precisely set at the minimum level necessary to maintain effective perfusion pressure. Indeed, the reflex response of the peripheral vascular bed may be so exaggerated that arterial pressure rises above control levels despite a considerable reduction in cardiac output. Thus the diseased ventricle is asked to generate a normal or greater than normal systolic wall tension at a time when its contractile force is impaired and a lower than normal arterial pressure would be better tolerated. The result may be a further reduction in ejection fraction and stroke volume which could initiate a vicious cycle characterized by a progressive reduction in cardiac output and a progressive increase in impedance. If sodium retention, reflex cardiac stimulation, and other negative feedback loops succeed in stabilizing the cardiac output, a state of chronic heart failure will exist; continuation of the vicious cycle may eventuate in the syndrome of shock.

A variety of vasodilator agents have been demonstrated to reverse some of the hemodynamic abnormalities of heart failure. Acute administration of sodium nitroprusside, phenolamine or nitroglycerin results in a sharp reduction in left ventricular filling pressure and an increase in cardiac output. The magnitude of the rise in cardiac output tends to be directly related to the degree of its initial depression. When the output is normal, as in some patients with acute myocardial infarction, little change occurs during vasodilator therapy. On the other hand, when cardiac output is markedly depressed, it may be increased to normal levels during treatment. In a series of patients with chronic intractable low output heart failure due to coronary artery disease or cardiomyopathy who were treated with intravenous sodium nitroprusside, cardiac output was nearly doubled, urine flow increased and the signs and symptoms of heart failure were relieved. The increase in stroke volume which accompanies vasodilator therapy tends to counterbalance the fall in systemic vascular resistance so that the reduction in mean arterial pressure is surprisingly small, and in some patients pressure recovers to pretreatment levels during continuous therapy. Thus a new steady state may be generated in which cardiac output is higher and impedance lower at nearly the same arterial pressure. Furthermore, heart rate usually does not rise but instead may fall as a manifestation of the circulatory improvement. The heart rate response may depend on the vasodilator drug employed, although definitive data on this point are not yet available.

The fall in left ventricular filling pressure which accompanies the vasodilator effect in heart failure requires closer scrutiny. Some of this response could represent an increase in ventricular compliance, but it also is likely that ventricular end-diastolic volume falls, at least in patients with markedly dilated hearts. A decrease in left ventricular end-diastolic volume could represent the combined effect of an increased ejection fraction and some venous pooling because of dilation of the capacitance vessels. Indeed, it might be attractive to postulate that the augmentation of stroke volume is due at least in part to improved ventricular function resulting from a reduction of preload in the overstretched ventricle which might be operating on a “descending limb” of its Starling curve. However, it is unlikely that a reduction in preload is an important primary factor in the acute increase in stroke volume since comparable reductions in left ventricular filling pressure induced by venous occluding tourniquets or phlebotomy lowered cardiac output in the same patients in whom nitroprusside infusion increased it. Although a fall in ventricular preload certainly may have a salutary long-term effect on cardiac function, the immediate improvement in left ventricular performance probably must be attributed largely to a reduction in impedance to ejection.

Although individual vasodilator drugs may have unique circulatory effects, they all relax vascular smooth muscle. A reduction of arteriolar resistance will allow more rapid runoff from the arterial bed during systole (reduced resistive impedance) whereas relaxation of the smooth muscle in the larger arteries may modify their pressure-volume relationship (reduced compliant impedance). Furthermore, as described above, these agents also may dilate venous capacitance vessels.
vasodilation induced by some of the drugs could contribute to improved myocardial function, but since a similar hemodynamic response is observed in both ischemic and nonischemic heart disease, it is unlikely that improved coronary perfusion plays a dominant role in the immediate circulatory response to vasodilators.

The effect of vasodilator therapy on cardiac metabolism is more complex. A reduction in left ventricular volume at end-diastole, and particularly during systole, along with some reduction in systolic pressure, signifies a considerable fall in myocardial oxygen consumption. The oxygen cost to stroke volume ratio therefore should be markedly lowered. This reduction in myocardial oxygen needs could be particularly beneficial in acute myocardial infarction and ischemic heart disease, in which an imbalance between oxygen supply and demand may directly impair cardiac function. However, net improvement in myocardial metabolism depends on the balance between changes in myocardial oxygen delivery and oxygen consumption. A reflex increase in heart rate, as has been reported in some patients given phentolamine, could increase oxygen consumption and aggravate ischemia. The fall in aortic diastolic pressure during vasodilator therapy, even if small, could reduce coronary blood flow. Regardless of changes in total coronary flow, however, subendocardial perfusion might be favored by a fall in the elevated left ventricular diastolic pressure which directly inhibits subendocardial flow. Nonetheless, recent studies have suggested that the salutary effect of nitroglycerin on myocardial ischemia in experimental myocardial infarction can be enhanced by maintaining a constant aortic pressure. Thus, it is premature to determine whether pharmacological reduction of impedance in patients with acute myocardial infarction will have a net beneficial effect, even if arterial pressure falls slightly, or whether it is vital to maintain, or even increase coronary perfusion pressure by use of intraaortic balloon or external counterpulsation.

Data are not yet available to provide a comparison between the effects of conventional therapy (diuretics and inotropic drugs) and the effects of pharmacological reduction of impedance on the signs and symptoms of heart failure. Studies reported to date have been limited to intravenous administration of drugs for periods not exceeding 72 hours. The efficacy of long-term therapy would be considerably more difficult to demonstrate, but such studies eventually must be undertaken. Chronic treatment would require the development of a well-tolerated, potent, orally effective vasodilator which does not induce a reflex tachycardia. It is likely that a variety of chemical agents which might meet these requirements could be synthesized. Furthermore, it would be beneficial if the peripheral vasodilator action resulted in distribution of the increased blood flow to critical vascular beds which previously were underperfused.

The impressive preliminary results with vasodilator therapy in heart failure of diverse etiologies suggests that hypertension is a more important factor in cardiac decompensation than was previously recognized. Data from the Framingham study have revealed that hypertension is the most common risk factor in the development of heart failure. Indeed, the systolic pressure, which is a resultant of impedance to ejection, was more closely correlated with subsequent heart failure than the diastolic pressure. It may therefore be appropriate to consider arterial systolic pressure the vital variable in circulatory homeostasis. Marked elevations of arterial pressure due to high impedance may decompensate a mildly abnormal heart, as in hypertensive crisis, but modest increases in pressure or even normal pressures may precipitate clinical heart failure when the ventricle is ischemic or its function severely compromised. Further experience may considerably expand the already broad application of antihypertensive therapy in our adult population.

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