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Understanding Coronary Blood Flow The Wave of the Future

Blase A. Carabello, MD

Fick's principle states that oxygen consumption of an organ or organism is equal to the product of blood flow and oxygen extraction from the blood. Among all organs, the heart is unique in that oxygen extraction is constantly close to maximal. Thus, the only way that this metabolically demanding organ can increase oxygen consumption is by increasing coronary blood flow. In this aspect of oxygen delivery, the heart also is unique because most flow occurs in diastole instead of in systole. In other organs, blood flows down a pressure gradient from its arterial source through the resistance of the arterioles into the capillary bed and thence venous return. In the heart, the compression of the vasculature by its surrounding muscle during systole impedes flow so that while the pressure head for flow is maximum in systole, flow is maximum in diastole. Thus, a simple "vascular waterfall" model in which flow moves from highest to lowest pressure does not fully explain observed myocardial flow phenomena.

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In this week's *Circulation*, Davies et al¹ used computer analysis of recordings of blood flow and pressure to detect and quantify intracoronary waves and to study coronary flow events in normal subjects and those with left ventricular hypertrophy (LVH). Waves were generated from both ends of the coronary tree. Proximal waves moved forward; distal waves moved backward. In this schema, proximal "pushing" waves and distal suction waves accelerate forward blood flow, while proximal suction waves and distal pushing waves do the opposite. Although the authors consistently detected 6 waves, 2 were dominant: a forward-moving pushing wave and a backward-moving suction wave (although this wave moves proximally, it propels blood forward). The forward-moving pushing wave is generated by systolic pressure. It probably drives blood primarily into the epicardial coronaries where it might be stored until it is released for forward flow when the myocardium relaxes. The second important wave, typically the largest, is a suction wave generated by relaxation

of the left ventricle and is probably the main driver in diastolic coronary blood flow.

Coronary Blood Flow in Normal Subjects and Those With LVH

In normal subjects, endocardial blood flow exceeds epicardial flow, so the ratio of endocardial to epicardial blood flow is $\approx 1.2:1$.^{2,3} It is generally held that this distribution matches the nutrient requirements of the endocardium where wall stress higher than that of the epicardium increases endocardial oxygen demand. It has been known for decades that this distribution is reversed in the presence of concentric LVH, predisposing toward endocardial ischemia.²⁻⁵ Indeed, such ischemically mediated endocardial contractile dysfunction has been demonstrated.^{6,7} Furthermore, it is known that coronary flow reserve is reduced in LVH.⁸ Although normal myocardium can increase its flow 5- to 8-fold under stress, it can be reduced by $\geq 50\%$ in concentric LVH. This mechanism must play a role in the angina observed in some patients with LVH who also have normal epicardial coronary anatomy, although most patients with LVH and reduced flow reserve do not develop angina. Explanations for reduced endocardial flow and reduced flow reserve in LVH have centered around reduced capillary density per unit of myocardium⁹ and increased resistance to flow. Decreased capillary density in LVH presumably occurs because capillary growth does not match muscle growth. Increased vascular resistance might occur because the hypertrophied left ventricle requires a higher filling pressure than normal, and higher diastolic filling pressure compresses the endocardium and impeded coronary blood flow,⁷ although not all investigators have found this explanation plausible.¹⁰ Alternatively, compromised vasodilator function may be responsible for increased coronary vascular resistance in LVH.¹¹

Davies et al¹ offer another plausible explanation for reduced flow in LVH. They found that although the forward-pushing wave was increased in their LVH patients, the backward-moving suction wave primarily responsible for diastolic coronary blood flow was reduced in comparison. The enhanced forward-pushing wave may have been due to higher systolic blood pressure in the LVH group. Although there was no statistical difference in blood pressure between the groups, there may have been differences during some of the measurements because hypertension was the likely cause of LVH in that group. However, the blunted suction wave implies a lusitropic deficit. Although no data regarding ventricular function were presented, intrinsic diastolic dysfunction is extremely common in patients with LVH. In addition, it can be speculated that this problem in relaxation was compounded by a contractile deficit not detected by

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insensitive measures of function such as ejection fraction. It is well known that subnormal sarcomere shortening in LVH can achieve normal ejection fraction as a result of enhanced thickening of concentrically hypertrophied ventricles.¹² In turn, subnormal contractile function (despite normal ejection fraction) would have reduced LV restoring forces, impairing relaxation and presumably blunting the diastolic suction wave. As LVH increases and left ventricular function worsens, it could easily set up a vicious cycle of reduced flow leading to impaired function leading to reduced flow, etc. The reversal in these changes could lead to improvement after the regression of hypertrophy when pressure overload is relieved.^{13,14}

The presence of LVH is a risk factor for congestive heart failure and for mortality in patients suffering a myocardial infarction. Abnormal coronary blood flow, especially to the endocardium, likely plays a role in this risk. Although blood flow usually is thought of in terms of driving pressure and vascular resistance, the complexities of coronary flow do not follow this simple logic. The present data help us look at coronary flow, especially in LVH, in a new and useful light. Future experiments examining how known acute alterations in ventricular function affect the waves reported in this issue will be of great interest.

Disclosures

None.

References

1. Davies JE, Whinnett ZI, Francis DP, Manisty CH, Aguado-Sierra J, Willson K, Foale RA, Malik IS, Hughes AD, Parker KH, Mayet J. Evidence of a dominant backward-propagating "suction" wave responsible for diastolic coronary filling in humans, attenuated in left ventricular hypertrophy. *Circulation*. 2006;113:1768–1778.

2. Rembert JC, Kleinman LH, Fedor JM, Wechsler AS, Greenfield JC Jr. Myocardial blood flow distribution in concentric left ventricular hypertrophy. *J Clin Invest*. 1978;62:379–386.
3. Bache RJ. Effects of hypertrophy on the coronary circulation. *Prog Cardiovasc Dis*. 1988;30:403–440.
4. Bache RJ, Vrobel TR, Arentzen CE, Ringh WS. Effect of maximal coronary vasodilation on transmural myocardial perfusion during tachycardia in dogs with ventricular hypertrophy. *Circ Res*. 1981;49:742–750.
5. Isoyama S, Ito N, Kuroha M, Takishima T. Complete reversibility of physiological coronary vascular abnormalities in hypertrophied hearts produced by pressure-overload in the rat. *J Clin Invest*. 1989;84:288–294.
6. Fujii AM, Gelpi RJ, Mirsky I, Vatner SF. Systolic and diastolic dysfunction during atrial pacing in conscious dogs with left ventricular hypertrophy. *Circ Res*. 1988;62:462–470.
7. Nakano K, Corin WK, Spann JF Jr, Biederman RWW, Denslow S, Carabello BA. Abnormal subendocardial blood flow in pressure overload hypertrophy is associated with pacing-induced subendocardial dysfunction. *Cir Res*. 1989;65:1555–1564.
8. Marcus ML, Doty DB, Hiratzka LF, Wright CB, Eastham CL. Decreased coronary reserve: a mechanism for angina pectoris in patients with aortic stenosis and normal coronary arteries. *N Engl J Med*. 1982;307:1362–1366.
9. Breisch EA, Houser SR, Carey RA, Spann JF, Bove AA. Myocardial blood flow and capillary density in chronic pressure overload of the feline left ventricle. *Cardiovasc Res*. 1980;14:469–475.
10. Canby CA, Tomanek RJ. Role of lowering arterial pressure on maximal coronary flow with and without regression of cardiac hypertrophy. *Am J Physiol Heart Circ Physiol*. 1989;257:H1110–H1118.
11. Tesfamarian B, Halpern W. Endothelium-dependent and endothelium-independent vasodilation in resistance arteries from hypertensive rats. *Hypertension*. 1988;11:440–444.
12. de Simone G, Devereux RB, DeLentano A, Roman MJ. Left ventricular chamber and wall mechanics in the presence of concentric geometry. *J Hypertens*. 1999;17:1001–1006.
13. Ishihara K, Zile MR, Nagatsu M, Nakano K, Tomita M, Kanazawa S, Clamp L, DeFreyte G, Carabello BA. Coronary blood flow after the regression of pressure-overload left ventricular hypertrophy. *Cir Res*. 1992;71:1472–1481.
14. Hildick-Smith DJ, Shapiro LM. Coronary flow reserve improves after aortic valve replacement for aortic stenosis: an adenosine transthoracic echocardiography study. *J Am Coll Cardiol*. 2000;36:1889–1896.

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