Correlation Between Acute Reductions in Myocardial Blood Flow and Function in Conscious Dogs

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This pioneering article was the first to quantitatively relate regional myocardial blood flow (microspheres) to regional contractile function (sonomicrometry). Regional flow and function were more or less proportionately reduced during acute ischemia in conscious dogs.

The notion that myocardial ischemia arises from an imbalance between oxygen demand and supply goes originally back to the characterization of hemodynamic determinants of myocardial oxygen consumption in the whole heart and the observation that decreases or increases, respectively, in heart rate or ventricular function decrease or increase, respectively, the severity of ischemic injury. However, myocardial ischemia is in most instances a regional event. It was not until into the 1970s that experimental techniques became available to measure myocardial blood flow and contractile function on a regional level, notably the microsphere technique and sonomicrometry. Stephen Vatner in his classic article was the first to use both techniques simultaneously and quantitatively relate subendocardial segment shortening to subendocardial blood flow. He characterized the flow–function relationship as exponential during acute coronary stenosis in conscious dogs, with a more steep and almost linear part at more severe stenosis. Admittedly, the measurements were restricted to only the subendocardial layer, and segment length measurements are somewhat technically limited by the alignment of piezocrystals with respect to myofiber direction. Nevertheless, flow–function relationships were subsequently reported from other groups for transmural flow and function, using more chronic coronary stenosis and extending the data from rest to exercise. Whereas initially there were heated debates on the exact shape of the flow–function plot and the potential meaning of its deviation from linearity, the prevailing view emerged that in (sub)acute ischemia regional myocardial blood flow and function are proportionately reduced (Figure) and not in imbalance, contrary to the above notion that ischemia is characterized by an imbalance of oxygen supply and demand. John Ross developed the concept of perfusion–contraction matching in which the observed reduction in contractile function is not the energetic consequence of reduced blood flow but an adaptive response. Perfusion–contraction matching can be maintained over hours of (sub)acute ischemia, and all drugs that attenuate ischemia operate along the flow–function relationship. With increasing duration of ischemia, perfusion–contraction matching is progressively lost.

The pathophysiological concept of perfusion–contraction matching coincided with the clinical observation of hibernating myocardium by Shahbudin Rahimtoola, and the idea emerged that indeed perfusion–contraction matching permits adaptation of the myocardium to ischemia and, in consequence, maintenance of its viability and eventual recovery after revascularization. Indeed, perfusion–contraction matching is a hallmark of hibernation. In short-term hibernation, the adaptation is biochemical/metabolic in nature, and only a short-term deviation from the flow–function relationship is possible with the recruitment of an inotropic reserve, however, at the expense of metabolic reserve. Long-term hibernation develops when repetitive bouts of stress-induced ischemia/reperfusion in the presence of chronic coronary stenosis and limited coronary reserve induce the upregulation of an adaptive molecular program that results in alterations in metabolism, reduced contractile function, and a matched reduction in blood flow. In contrast to hibernation, stunning is characterized by a...
dissociation of normalized or only slightly reduced blood flow and persistent, yet reversible, contractile dysfunction during reperfusion after myocardial ischemia, that is, perfusion–contraction mismatch.22 Stunning is a result of increased formation of reactive oxygen species23–25 and calcium overload during reperfusion, which impair excitation–contraction coupling.26,27 It seems that long-term hibernation develops from cumulative episodes of acute stunning in a continuum that is initially characterized by a mismatch of flow and function (as in acute stunning) and then progresses into a new match (as in short-term hibernation).28,29 Another manifestation of perfusion–contraction mismatch arises from spontaneous or interventional coronary microembolization,30 where blood flow is normal or slightly elevated (reactive hyperemia), but contractile function is severely depressed as a result of patchy microinfarcts and an inflammatory reaction with cytokine-induced and reactive oxygen species–mediated impairment of the contractile machinery.31–33

Perfusion–contraction match and mismatch are not only of conceptual academic interest, but have also become important criteria in modern cardiovascular imaging to guide decisions on coronary revascularization.34 As one sees from the references, most of the original studies in the field have been reported in Circulation Research and much of the conceptual debate35,36 has happened here. The current editor is the best guarantee that Circulation Research will continue to be the forum for integrative hemodynamic research as it has been under his predecessor, whose classic article I have had the pleasure to comment on.

Disclosures

None.

References


The Regional Myocardial Flow–Function Relationship: A Framework for an Understanding of Acute Ischemia, Hibernation, Stunning and Coronary Microembolization
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