Transmural adenosine with increased cardiac work

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Summary

In hearts with five different levels of myocardial performance there was an inverse correlation between myocardial adenosine content and coronary vascular resistance. Higher levels of oxygen consumption were associated with higher myocardial adenosine content and lower coronary vascular resistance. Adenosine was uniformly distributed across the myocardial wall under all conditions, except those involving increased oxygen consumption with concomitant decreased coronary input pressure, as was observed with isoproterenol infusion. Under these conditions the adenosine content of the inner wall was significantly higher than the outer wall.

Several investigators have demonstrated that myocardial adenosine content and release are increased under conditions of decreased myocardial oxygen supply (2, 4). However, the evidence supporting a role for adenosine in the regulation of coronary blood flow during increased myocardial oxygen consumption is limited (5). Under physiological conditions, myocardial oxygen supply is regulated in response to changes in myocardial oxygen demand. Therefore, to support the hypothesis that adenosine regulates coronary vascular resistance, it is important to demonstrate an inverse relationship between myocardial adenosine content and coronary vascular resistance during conditions of increased myocardial oxygen consumption.

Moreover, since transmural pressure gradients develop during contraction, the intramyocardial pressure of the inner wall may exceed coronary perfusion pressure during systole, limiting blood flow to the inner wall while the outer wall is adequately perfused. The resulting underperfusion of the inner wall during systole is compensated for during diastole, since vascular resistances and blood flows in the inner and outer walls of the myocardium are equal when averaged over several cardiac cycles (3). The compensation may result from greater production of a vasodilator, such as adenosine, in the inner wall during systole, allowing for greater blood flow during diastole. The following models were developed to examine the relationship between myocardial adenosine content and coronary vascular resistance in the total myocardium and transmurally across the myocardium during conditions of increased myocardial oxygen consumption.
Methods and materials

We examined two dog models, the anesthetized, open-chest model and the unanesthetized closed-chest model.

In the open-chest model, dogs were anesthetized and catheters were placed in the left ventricle and aorta for pressure measurements, and in the left femoral artery and coronary sinus for withdrawal of blood. Coronary blood flow was measured with 15 µ radioative microspheres. Three groups were studied: a control group, an aortic-constricted group in which we gradually constricted the ascending aorta to produce a 50% increase in peak systolic intraventricular pressure, and an isoproterenol-infused group in which isoproterenol hydrochloride was infused intravenously at 0.32 to 0.64 µg/min/kg. At the end of a 15-minute period in all groups, a transmural drill biopsy of the left ventricle was rapidly removed and frozen with Wollenburger tongs precooled in liquid nitrogen.

In the unanesthetized closed-chest model, the fifth rib was removed and the pericardium pulled against the chest wall as the incision was closed. Following a nine-day recovery period, control animals rested in a sling mounted above a treadmill, while exercising animals ran at 8 kilometers/hour on a 20% slope for 7 min. At this time, sodium thiamylal was rapidly injected through a carotid artery catheter directed cephalad producing virtually instantaneous central anesthesia.

![Graph showing relationship between log of myocardial adenosine content and coronary vascular resistance.](image_url)

Fig. 1. Relationship between log of myocardial adenosine content and coronary vascular resistance. Each point represents the mean of the group. Values for resistance and adenosine content are mean values for the left ventricle.