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Adenosine Receptor Blockade Enhances Myocardial Stunning Without a Sustained Effect on Fluorine-18-FDG Uptake Postreperfusion

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The aim of this study was to determine whether adenosine receptor blockade before ischemia would enhance the degree of stunning and induce a sustained decrease in glucose uptake after reperfusion. **Methods:** Stunning was induced in 14 anesthetized swine by partially occluding the left anterior descending artery (LAD) for 20 min (> 80% flow reduction). Seven animals were pretreated with the nonspecific adenosine receptor blocker 8-phenyltheophylline (8-PT; 5 mg/kg), which decreased reactive hyperemia by an average of 38%. Myocardial glucose uptake was assessed 1 hr following reperfusion with PET and the glucose analog ^{18}F-fluorodeoxyglucose (FDG). **Results:** Before ischemia, systolic shortening in the LAD region was 15% ± 6% in the control group and 16% ± 4% in the 8-PT group and in both groups was reduced to − 1% ± 2% during ischemia. After reperfusion, systolic shortening was 7% ± 3% in the control group and 2% ± 3% in the 8-PT group ($p < 0.05$). Myocardial oxygen consumption before ischemia was 4.58 ± 3.03 μmol/min/g in the control group and 4.44 ± 1.83 μmol/min/g in the 8-PT group (ns) and neither were different after reperfusion. In the postischemic LAD region, myocardial glucose uptake was 0.18 ± 0.15 μmol/min/g in the control group and was similar to that of the 8-PT group (0.17 ± 0.08 μmol/min/g; ns). **Conclusion:** The nonspecific adenosine blocker 8-PT enhanced the degree of stunning when given before ischemia but did not induce a sustained effect on myocardial glucose uptake after reperfusion.

Key Words: PET; fluorine-18-fluorodexoyglucose; stunning; adenosine; glucose; metabolism; reperfusion injury

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Exogenous adenosine protects the myocardium from ischemic injury. When administered before prolonged periods of ischemia, it prevents necrosis by initiating a preconditioning cascade through the A_1 receptor (*1*). When administered during early reperfusion, it restores perfusion and prevents "no-reflow," potentially through the A_2 receptor (*2,3*). During brief periods of ischemia, augmenting endogenous levels of adenosine also may be protective by attenuating the degree of stunning (*4–7*). Although the mechanism of this observation is complex, one possibility is that adenosine receptor stimulation could alter metabolism favorably, either during ischemia by decreasing oxygen demands (*8*) or after reperfusion, by increasing glucose uptake (*9*). Enhanced glucose uptake during early reperfusion may be protective by maintaining calcium homeostasis (*10*) and this in turn may be modulated by adenosine (*9,11–13*). Accordingly, the aim of this study was to determine whether 8-phenyltheophylline (8-PT), a nonselective adenosine receptor blocker, enhances the degree of stunning while decreasing glucose uptake postreperfusion. Anesthetized swine were used for these studies and myocardial glucose uptake was measured by PET and the glucose analog ^{18}F-fluorodeoxyglucose (FDG).

MATERIALS AND METHODS

This study was performed under the guidance of the Animal Care Committee at the VA Medical Center, Minneapolis, MN and conforms with U.S. National Institutes of Health Publication No. 85-23 (*14*).

Animal Preparation

Fasted swine of either sex (30–38 kg) were sedated with ketamine (20 mg/kg; intramuscular) and pentobarbitone (10 mg/kg; intravenous) infused into an ear vein. They were intubated, connected to a respirator and ventilated with oxygen-enriched air to maintain normal arterial pH (7.35–7.45), pCO_2 (35–45 mm Hg) and pO_2 (>100 mm Hg). The left external jugular vein and internal carotid artery were exposed and cannulated with 7F catheters. Anesthesia was initiated with a bolus of alpha chloralose (150 mg/kg; intravenous) supplemented with an infusion of sodium pentobarbitone (5 mg/kg/hr). The right femoral artery was exposed and cannulated with a 7F catheter and used for blood sampling and blood pressure measurement.

After administration of succinyl choline (0.25 mg; intravenous), a midline sternotomy was performed and the heart was suspended

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in a pericardial cradle. The left mammary vessels were ligated and the left second rib was removed for ease of further instrumentation. A 7F catheter was secured into the left atrium and used for administration of radiolabeled microspheres. A proximal portion of the left anterior descending coronary artery (LAD) was isolated and a Doppler flow probe (3.0 mm) placed just proximal to a hydraulic occluder. A 5F Millar catheter was inserted into the left ventricle (LV) through the apex and used for measurement of LV pressure and its first derivative [first derivative of LV pressure (dP/dt)]. A 22F intracatheter was inserted into the great cardiac LAD vein just distal to the occlusion site of the LAD.

Regional segment length shortening was measured in the distribution of the LAD artery using a pair of endocardial ultrasonic crystals. Systolic shortening was calculated from the difference between lengths at end-diastole (time of onset of positive dP/dt) and end-systole (time of peak negative dP/dt) and expressed as a percent of end-diastolic length. Meticulous attention was made to ensure that placement and crystal alignment were not altered during the experimental protocol. In all animals, dextrose (25 g) was infused intravenously 1 hr before the experimental protocol to stimulate the release of endogenous insulin and ensure myocardial uptake of the glucose tracer.

Regional Myocardial Blood Flow

At baseline and 30 min after reperfusion, 1–2 million microspheres (15 μ) labeled with either ^{141}Ce, ^{113}Sn, ^{103}Ru, or ^{95}Nb were injected into the left atrium. Reference arterial blood samples were withdrawn from the femoral artery catheter at a fixed rate of 10 ml/min, beginning 5 sec before and for 2 min after microsphere injection. At the conclusion of the experiment and before killing, the distribution of the postischemic myocardium was identified by injecting blue dye into the left atrium during LAD occlusion. Hearts were fixed in 10% formalin for at least 48 hr, and separated into LAD and non-LAD regions. Each region was then sudivided into three layers of equal thickness (inner, mid and outer). Myocardial and reference blood samples were counted in a multichannel analyzer (Gamma Counter-5000; Packard Instrument, Inc., Downers Grove, IL) and regional blood flows were determined.

Blood gas analyses, oxygen saturations and hemoglobin content from arterial and venous blood samples were calculated by a pH analyzer (Model 278; Chiron Diagnostics, Inc., Medfield, MA). Lactate and glucose concentrations were determined from aliquots of 3 ml of blood that were transferred into iced-glass tubes for later analysis by enzymatic technique. Oxygen consumptions were computed from the product of myocardial blood flows and arterial-venous oxygen differences.

Experimental Protocol

Of 14 animals, 7 were used as a control group and 7 were pretreated with 8-PT (Sigma Chemical, St. Louis, MO). The 8-PT (5 mg/kg) was diluted in 3 ml dimethol sulfoxide (DMSO), 3 ml 0.5 *M* NaOH and 3 ml 0.1 *M* NaOH and during gentle heating with stirring, mixed with NaCl for a total volume of 30 ml. In pigs anesthetized with the same agents as in this study, this dose has been shown to blunt the hyperemic effect of exogenously administered adenosine for at least 2 hr postadministration (*15*). The 8-PT was infused intravenously over 5 min. Five minutes before and 5 min after the infusion, reactive hyperemia was measured in all animals by measuring the integral of the mean coronary blood flow response to a 30-sec occlusion. After administering the 8-PT, the reactive hyperemia was reduced by a mean of 38% (28%–48%), demonstrating blockade of the adenosine A_2 receptor with the nonspecific adenosine blocker (*16*).

Animals were stabilized for 10 min and baseline recordings were obtained, whole blood samples were withdrawn from the aorta and great cardiac LAD vein for oxygen contents and radiolabeled microspheres were injected. Using the hydraulic occluder and the mean Doppler flow recordings, coronary blood flow in the LAD artery was reduced by 80% for a total of 20 min. This degree of ischemia is sufficient to induce severe stunning and minimizes the ventricular fibrillation that might occur during total coronary artery occlusion (*17*). The occluder then was released and the LAD region reperfused for 30 min. At that time, recordings were obtained, simultaneous aortic and coronary venous samples were withdrawn and a second set of microspheres was injected. Animals then were transported to the PET scanning room. Although function could not be measured beyond 30 min of reperfusion, earlier studies have shown that differences in postischemic function between 8-PT-treated and control animals remain constant between 30 and 60 min of reperfusion (*18*).

PET Scanning Procedures

These studies used an ECAT 953B/31 (CTI/Siemens, Inc., Knoxville, TN), which is capable of rapid dynamic imaging. The camera consists of 16 contiguous rings of bismuth germinate detectors allowing acquisition of 31 cross-sectional images of the heart simultaneously recorded in a 10.8-cm axial field of view. In a transaxial resolution, a 5.8-mm FWHM would be expected at the center of the field of view. Emission images were reconstructed using a Hanning filter with a cutoff frequency of 0.4 of maximum (0–0.5 scale). The effective transaxial resolution of the reconstructed images is 10 mm.

Animals were placed on the table and, positioned using a laser light detector, so that the heart was in the center of the field of view. Attenuation of tissue density for subsequent ^{18}F-FDG images was accomplished by a 10-min transmission scan using an internal source of radiation. Fluorine-18-FDG (5 mCi) was infused intravenously over 20–30 sec and the dynamic scans were acquired using a scanning protocol of twelve 10-sec, six 30-sec, four 60-sec, three 2-min, three 5-min and one 10-min frames.

Data Analysis

Regions of interest (ROIs) from the myocardium were selected from 10–12 planes of the final frame of the ^{18}F-FDG scan (primarily myocardial image). Fifteen to 20 circular-tissue ROIs were defined within both LAD and non-LAD regions. One ROI from the largest portion of the left ventricular chamber was defined as arterial input and together with the tissue ROIs, used to generate time-activity curves for subsequent analysis.

Myocardial glucose uptake was quantitated for both the LAD and non-LAD regions by Patlak analysis of regional time-activity curves. Based on a three-compartment model that incorporates the forward (k_1) and reverse (k_2) rate constants from plasma to tissue and the phosphorylation and dephosphorylation rate constants (k_3 and k_4, respectively), the Patlak plot defines a constant (K), which is comprised of the individual constants $(k_1 \times k_2)/(k_2 + k_3)$. In these analyses, k_4 is assumed to be zero. The lumped constant corrects for differences in transport and phosphorylation rates between glucose and ^{18}F-FDG and is assumed to be 0.67. Glucose uptake can then be calculated by the product of plasma glucose concentration and the constant K divided by the lumped constant 0.67 (*19–21*).

Statistics

Results are expressed as arithmetic means ± standard means. Intergroup differences were tested for significance at the $p < 0.05$ level by paired Student's t-test. Repeated measures were tested by ANOVA with Fisher's protected least significant difference (PLSD).

TABLE 1
Systemic Hemodynamics in Control Group and 8-Phenyltheophylline (8-PT) Pretreated Swine

	Heart rate (bpm)	Mean arterial pressure (mmHg)	LV dP/dt_{max} (mmHg/sec)	LV EDP (mmHg)
Baseline				
Control	116 ± 16	94 ± 7	2057 ± 577	10 ± 2
8-PT	114 ± 22	101 ± 21	1943 ± 299	12 ± 5
Post-8PT				
Control	na	na	na	na
8-PT	137 ± 25†	107 ± 18	1971 ± 315	13 ± 4
Ischemia				
Control	110 ± 14	86 ± 12	1371 ± 450†	16 ± 14†
8-PT	130 ± 19*†	98 ± 22	1571 ± 335†	18 ± 6†
Reperfusion				
Control	108 ± 18	92 ± 12	1457 ± 411†	12 ± 4
8-PT	129 ± 15*†	96 ± 17	1671 ± 287†	13 ± 4

*$p < 0.05$ vs. control group.
†$p < 0.05$ vs. baseline.
8-PT was infused intravenously in a dose of 5 mg/kg approximately 10 min before ischemia. Means ± s.d.; n = 7 per group; na = not applicable; LV = left ventricle; EDP = end-diastolic pressure.

RESULTS

Systemic Hemodynamics

Table 1 summarizes the systemic hemodynamics for both the control and 8-PT pretreated animals. At baseline, there were no intergroup differences in heart rate, mean arterial blood pressure, LV dP/dt_{max} or LV end-diastolic pressure. After administration of 8-PT, heart rate increased from 114 ± 22 bpm to 137 ± 25 bpm ($p < 0.05$) and this increase was sustained for the remainder of the protocol. For both groups, ischemia induced a significant decrease in LV dP/dt_{max} and a significant increase in LV end-diastolic pressure when compared with baseline values.

Regional Segment Length Shortening

At baseline, systolic shortening was 15% ± 6% in the control group and 17% ± 4% in the 8-PT group. Ten minutes after drug administration and just before ischemia, shortening in the treatment group was 16% ± 4% (ns). As shown in Figure 1, ischemia induced similar reductions in regional function in both groups with net bulging noted. After reperfusion, systolic shortening was significantly depressed in all animals compared with preischemic values, however a greater degree of stunning was noted in the 8-PT group compared with the control group (2% ± 3% versus 7% ± 3%, respectively; $p < 0.05$). To determine how much of an effect the small increase in heart rate may have had during ischemia, a regression fit was done between heart rate during ischemia and the degree of stunning. There was no significant correlation between the two parameters in either group ($r = 0.27$; $p = 0.56$ and $r = 0.33$; $p = 0.47$ in control and 8-PT animals, respectively), which suggests that the small difference in heart rate (~20 bpm) is unlikely to have induced the large difference in postischemic systolic shortening between control and 8-PT animals.

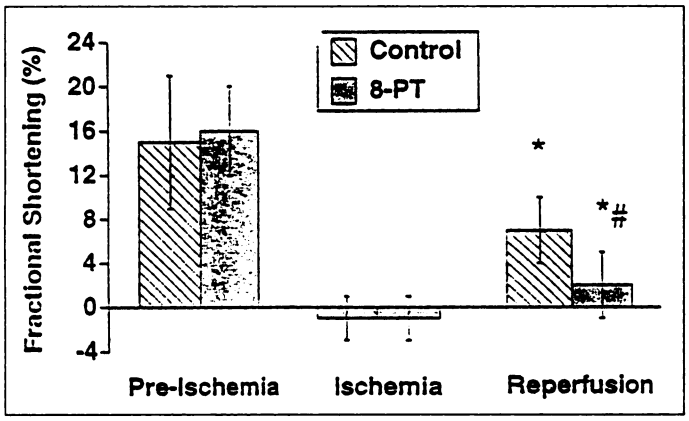

FIGURE 1. Systolic fractional shortening (%) in the left anterior descending artery region is shown in the control group and in animals pretreated with 8-phenyltheophylline (8-PT) before, during and 30 min after ischemia. The results show that the degree of stunning was greater in the 8-PT animals compared with the control group. Means ± s.d.; *$p < 0.05$ vs. pre-ischemia; #$p < 0.05$ vs. control.

Myocardial Blood Flow and Metabolism Poststunning

The effects of ischemia and reperfusion on myocardial blood flow, MVO_2 and lactate uptake in the LAD region of both groups are shown in Table 2. Before ischemia, myocardial blood flow in the LAD region was 1.05 ± 0.54 ml/min/g in the control group and 1.14 ± 0.17 ml/min/g in the 8-PT group (ns). After stunning, endo/epi ratios in the postischemic LAD regions were 1.02 ± 0.15 in the control group and 1.01 ± 0.07 in the 8-PT groups and neither differed from preischemic values. In the control group, coronary blood flow by Doppler was reduced from 26 ± 9 ml/min to 4 ± 1 ml/min during ischemia while in the 8-PT group, it was reduced from 38 ± 14 ml/min to 5 ± 2 ml/min during ischemia. This represented equivalent degrees of flow reduction for both groups. Before ischemia, MVO_2 was 4.58 ± 3.03 μmol/min/g in the control group and 4.44 ± 1.83 μmol/min/g in the 8-PT group (ns) and both were slightly decreased after reperfusion. Lactate uptake was similar in both groups before ischemia and equally reduced after stunning.

Myocardial glucose uptake was estimated by ^{18}F-FDG kinetic studies after reperfusion in both groups. During the PET scan, plasma glucose was 6.9 ± 2.8 μmol/ml in the control group and 6.2 ± 1.0 μmol/ml in the 8-PT group (ns). At the same time, plasma lactate was 1.3 ± 0.3 μmol/ml in the control group and 1.3 ± 0.4 μmol/ml in the 8-PT group (ns). After reperfusion, myocardial glucose uptake in the LAD region of the control and 8-PT groups was 0.18 ± 0.15 μmol/min/g and 0.17 ± 0.08 μmol/min/g, respectively (ns) and those values were significantly lower than those observed in remote regions (Fig. 2).

DISCUSSION

Adenosine receptor stimulation by exogenously administered adenosine has been shown to be cardioprotective in several

TABLE 2
Myocardial Blood Flow, MVO_2 and Lactate Uptake in the Left Anterior Descending Artery Region of Control and 8-Phenyltheophylline (8-PT) Pretreated Swine

	Myocardial blood flow (ml/min/g)		MVO_2 (μmol/min/g)		Lactate uptake (μmol/min/g)	
	Preischemia	Reperfusion	Preischemia	Reperfusion	Preischemia	Reperfusion
Control	1.05 ± 0.54	0.91 ± 0.05	4.58 ± 3.03	2.84 ± 0.82	0.57 ± 0.65	0.08 ± 0.16*
8-PT	1.14 ± 0.17	1.05 ± 0.17	4.44 ± 1.83	3.59 ± 0.93	0.58 ± 0.21	0.15 ± 0.16*

*$p < 0.05$ vs. preischemia
8-PT was infused intravenously in a dose of 5 mg/kg approximately 10 min before ischemia. Means ± s.d.; n = 7 per group.

animal models of ischemia and reperfusion. This can be initiated either before ischemia, through the A_1 receptor and the preconditioning cascade (*1*) or during early reperfusion, through the A_2 receptor and improved reflow (*2*). In this study, a brief period of ischemia was used to test whether endogenous adenosine attenuates postischemic dysfunction (stunning). In swine pretreated with the nonspecific adenosine receptor blocker 8-PT, a greater degree of stunning was noted compared with control animals subjected to the same protocol. An infusion of 5 mg/kg over 5 min was used, which was sufficient to blunt reactive hyperemia by ~38%. This is consistent with the degree of hyperemia that might be expected from endogenous adenosine release after brief ischemia (*16,22,23*). We also have shown that the cardioprotective effects of adenosine were not associated with sustained changes in one component of glucose metabolism, namely regional myocardial glucose uptake.

Tissue Adenosine and Stunning

One strategy to test the cardioprotective effects of adenosine on stunning has been to augment endogenous levels with inhibitors of adenosine deaminase. In isolated hearts pretreated with either erythro-9-(2-hydroxy-3-nonyl)adenine (EHNA) (*24*) or 2-deoxycoformycin (*25*), the recovery of function was more complete after a brief period of ischemia when compared with control animals. Similar findings were noted in anesthetized dogs pretreated with EHNA, which markedly increased interstitial adenosine levels during 15 min of ischemia and reperfusion and was associated with less stunning (*4*). Tissue concentrations of adenosine also can be increased by inhibiting nucleoside transport, which prevents adenosine from being transported into endothelial cells for subsequent catabolism. In anesthetized dogs, intracoronary administration of this class of drug attenuated the degree of stunning after multiple short episodes of ischemia and reperfusion (*5*). The combination of EHNA and a selective inhibitor of nucleoside transport showed a sixfold increase in tissue adenosine during ischemia and twofold increase after reperfusion (*7*). As with prior studies, this effect was associated with less stunning when compared with nontreated animals subjected to the same protocol. Interestingly, no intergroup differences were noted in postischemic myocardial ATP levels which provide additional evidence that substrate repletion with adenosine is not the mechanism of the improved function after stunning (*26*).

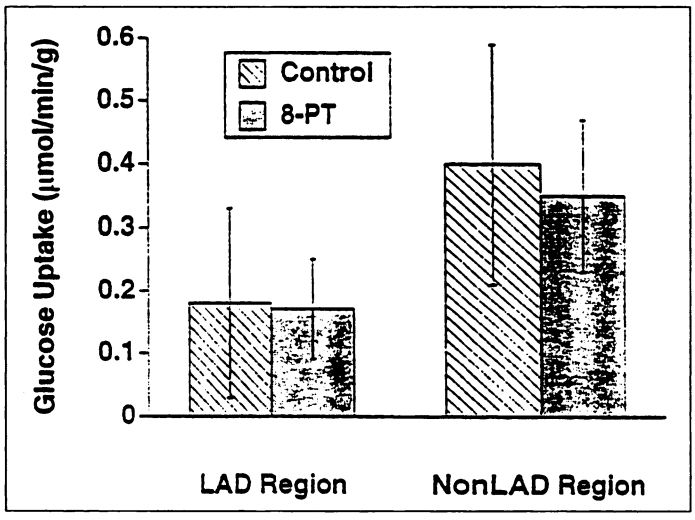

FIGURE 2. Myocardial glucose uptake by PET was determined in the control group and in animals pretreated with 8-phenyltheophylline (8-PT). There were no intergroup differences in glucose uptake in the postischemic region although the remote regions were higher in both groups. Means ± s.d. LAD = left anterior descending artery.

Adenosine Receptors and Stunning

The causes of the cardioprotective effects of adenosine in stunned myocardium are unclear but could involve the indirect actions of adenosine on preserved calcium homeostasis. Potential mechanisms include the prevention of xanthine oxidase-dependent generation of free radicals, the blocking of slow calcium channels and the inhibition of glycolysis which would lower intracellular pH and stimulate the sodium-calcium exchange current (*26*). On the basis of this study, the cardioprotective actions appear to be receptor mediated, though this has been controversial. It is possible that species differences can account to some extent for the conflicting results in the literature, however, more important considerations are the variable experimental designs including total time of ischemia, partial versus complete occlusions and receptor manipulation (stimulation versus blockade). In anesthetized dogs exposed to brief ischemia and reperfusion, the protective effects of alpha1-adrenergic mediated adenosine release was inhibited with the adenosine receptor blocker 8-PT (*6*). These findings are consistent with data from isolated rat hearts in which adenosine delayed the time of onset of contracture during low-flow ischemia, an effect which was inhibited by 8-PT (*27*). There is growing evidence that A_1 receptor stimulation plays an important role in protecting the myocardium against stunning. In anesthetized dogs subjected to multiple periods of ischemia and reperfusion, the A_1 agonist cyclopentyladenosine improved postischemic function when given before ischemia while pretreatment with the A_1 antagonist 8-cyclopentyl-1,3-dipropylxanthine increased the degree of stunning (*28*). Because this protective effect of the adenosine A_1 receptor could be blunted with glibenclamide, the involvement of ATP-dependent K channels was postulated. Although this would be an attractive link between mechanisms involved with preconditioning, several studies have convincingly dissociated stunned from preconditioned myocardium (*29,30*).

Adenosine and Metabolism

Adenosine could protect the myocardium against reperfusion injury by altering metabolism, either during ischemia or after reperfusion. As a modulator of metabolism, it has been shown to reduce myocardial contractility and the oxygen consumed for excitation-contraction coupling (*8*). This would have a favorable effect on the supply-demand mismatch during ischemia. In open chest cats exposed to 10 min of ischemia and reperfusion, pretreatment with 8-PT enhanced the degree of stunning as observed in this study (*18*). Adenosine also might be cardioprotective during ischemia by altering substrate utilization. It has been shown to increase glycolytic flux (*9*), which in turn could provide an additional source of ATP during levels of hypoperfusion (*31*). In models of low-flow ischemia, this may explain why adenosine preserves high-energy phosphates, increases tissue lactate content and delays the onset of contracture (*27,32*). It also may explain why endogenous adenosine during ischemia preserves metabolism after reperfusion (*33*). The net effect of adenosine on myocardial metabolism is controversial, however, particularly in regards to glucose. Although adenosine increases glucose uptake independent of changes in blood flow (*11*), this effect is only apparent during high insulin concentrations (*12*). Adenosine A_1 receptor stimulation has been implicated in this insulin-enhancing property, however, there are conflicting reports regarding the role of adenosine and glucose transport. In studies from isolated myocytes for instance, analogs of adenosine have been shown to inhibit glucose transport and decrease glucose utilization during hypoxia (*34*). This is more compatible with the results from isolated rat hearts, which have shown that adenosine protects the ischemic myocardium by inhibiting glycolysis and the accumulation of glycolytic byproducts and stimulating glucose oxidation (*13*).

In this study, we have confirmed that endogenous adenosine protects the myocardium after stunning without a sustained effect on glucose uptake. This does not necessarily imply that enhanced glucose uptake in the early phase of reperfusion is not an important factor in attenuating reperfusion injury (*10*). Because of the limitations of tracer kinetic studies, we are unable to measure substrate uptake during that dynamic period. However, this study does show that sustained effects on myocardial glucose uptake may not be evident, at a time that adenosine blockade has aggravated stunning. Although, the absence of intergroup differences in MVO_2 and lactate uptake suggests no sustained effects on substrate utilization, this may be difficult to conclude, due to the inherent variability of Fick measurements for estimating substrate uptake.

Methodological Considerations

Myocardial glucose uptake was estimated with PET and the glucose analog ^{18}F-FDG. The advantages of this technique are the improved spatial orientation for identifying postischemic myocardium and the use of tracer kinetic modeling, which is less subject to sampling error as might be expected with Fick measurements. The use of PET and ^{18}F-FDG have, however, distinct limitations. Most importantly, rates of myocardial ^{18}F-FDG uptake are only an estimate of glucose trapping and not glucose flux and, therefore, the relationship between glycogen storage, glycolysis and glucose oxidation cannot be determined. In addition, criticism has been raised over the use of the lumped constant, which in this study was assumed to be 0.67, based on previous validation studies (*19,35*). This constant accounts for differences in transport and phosphorylation between molecules of glucose and ^{18}F-FDG but may vary under altered metabolic conditions. This is unlikely to be a confounding variable in this study, however, because the experimental feeding conditions and levels of plasma glucose and lactate were identical in both groups. In regards to the effects of stunning, the lumped constant has not been shown to be affected by brief periods of ischemia and reperfusion in isolated hearts (*36*). An additional limitation of this study is that only one measurement of glucose uptake with PET was obtained. Although glucose uptake in the stunned regions was lower than the remote territory, this does not necessarily imply that glucose uptake was decreased poststunning. On the contrary, previous studies with PET have shown that ^{18}F-FDG uptake in stunned myocardium may be lower than remote regions but is not lower than preischemic baseline measurements (*37*).

In this study, rate-pressure product in the adenosine blocker group was higher than that of the control group during the ischemic period and we cannot exclude that such differences may have exacerbated intergroup differences in stunning. On the other hand, there was no correlation between stunning and either heart rate or double product in the pretreated group, which suggests that factors other than work load were responsible for the significant intergroup differences in stunning. Although we have shown that stunning was worse with adenosine blockade at one time point postreperfusion, we cannot comment on the effects of adenosine on the ultimate time course of recovery.

CONCLUSION

In this swine model of stunning, endogenous adenosine attenuated the degree of mechanical stunning by virtue of a receptor mediated mechanism. This effect was not associated with altered myocardial ^{18}F-FDG uptake with PET, suggesting that the observed cardioprotection did not involve sustained effects on glucose utilization after reperfusion.

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(continued from page 9A)

FIRST IMPRESSIONS
Technetium-99m-DTPA Images of Renal Cell Carcinoma Arising in a Crossed-Ectopic Fused Kidney

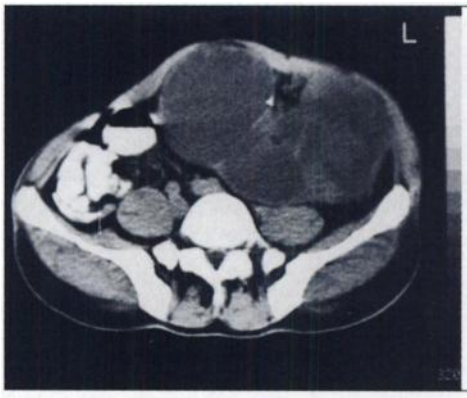

Figure 1.

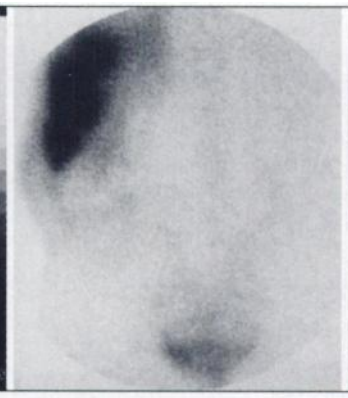

Figure 2.

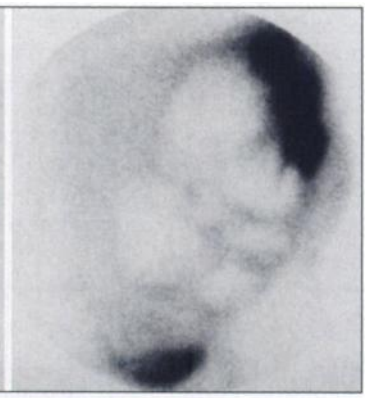

Figure 3.

PURPOSE
A 50-yr-old man with a several-week history of abdominal pain and hematuria was admitted to the hospital. A CT scan revealed a giant lobulated mass containing calcifications and liquid between the gastric fundus and pelvis (Fig. 1). The left kidney was seen cephalad to the mass. No right kidney could be detected. Intravenous pyelography showed dilated pelvic structures of the left kidney; no excretion was observed on the right side. An insignificant amount of contrast material was seen in the urinary bladder on the delayed radiograph images. A crossed-ectopic, probably hydronephrotic, fused kidney was diagnosed. A ^{99m}Tc-diethylenetriamine pentaacetic acid (DTPA) scan showed the left kidney displaced to the left upper quadrant and minimal bladder activity (Figs. 2 and 3, anterior). Surgery revealed a giant hydronephrotic fused kidney with solid and cystic components retaining more than 1000 cc blood and necrotic material. Histopathological examination revealed renal cell carcinoma of the fused kidney.

TRACER
Technetium-99m-DTPA (555 MBq)

ROUTE OF ADMINISTRATION
Intravenous

TIME AFTER INJECTION
35 min

INSTRUMENTATION
Starcam 4000I gamma camera (General Electric Medical Systems, Milwaukee, WI)

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