EVALUATION OF MYOCARDIAL PERFUSION AFTER INTRACORONARY INJECTION OF RADIOPOTASSIUM

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The feasibility of external imaging in dogs after coronary injection of potassium and its potential as an index of myocardial perfusion and viability were studied. The total myocardial extraction after intracoronary injection of potassium was 30–42%. The first-circuit myocardial extraction was 35–40%. Potassium was washed out of the myocardium with a half-time of 30 min, a rate sufficiently slow to permit external imaging for some time after injection. Images of normal myocardial perfusion in multiple projections were obtained after the intracoronary injection of ^{43}K with the Anger camera. The intracoronary injection of potassium permitted evaluation of a single coronary artery and its comparison with total myocardial perfusion.

When potassium and its analogs, rubidium and cesium, are introduced into the general circulation for imaging purposes, their dilution into the body fluids results in considerable background interference and relatively small concentration in the heart, which seriously limit their application to coronary artery disease. In addition, the small fraction of myocardial uptake from the allowable dose results in a low-photon yield.

By introducing potassium directly into the coronary vasculature, we have attempted to circumvent these shortcomings. In this study we investigated the feasibility of external imaging in dogs after intracoronary injection of potassium and its potential as an index of myocardial perfusion and viability.

METHOD

Rationale. The myocardial extraction of potassium and rubidium after intravenous injection was compared to determine whether ^{86}Rb could be used as a substitute for potassium. This was a necessary prerequisite because the first-circuit myocardial extraction required both intravenous and intracoronary injections of a potassium analog for quantification. Total and first-circuit myocardial extractions were measured after the intracoronary injection of potassium. In addition, we ascertained the rate of potassium efflux from the myocardium, after intracoronary injection, to determine whether sufficient potassium remains within the myocardium to permit further imaging. We have externally imaged the normal dog myocardium with the Anger scintillation camera after the intracoronary injection of ^{43}K to substantiate further our in vitro studies.

Isotopes. Potassium-42 has a half-life of 12.35 hr and emits a 1.524-MeV gamma ray with an 18% incidence. The specific activity of the ^{42}K used in these experiments was 145–254 mCi/gm; after dilution, prior to intracoronary injection, the concentration of potassium was 3.17–5.55 mEq/liter. Rubidium-86 emits a 1.078-MeV gamma ray (8.8% incidence) and has a half-life of 18.7 days.

Potassium-43* emits predominately two gamma rays, 373 keV (85%) and 619 keV (81%), and has a 22.4-hr half-life. Because the isotope is carrier free and contains less than 10% accompanying ^{42}K at the time of injection, the concentration of potassium injected into the coronary circulation is less than 10^{-6} mEq/liter.

Technique. Female mongrel dogs weighing 13–20 kg were used in all experiments. The animals were anesthetized with sodium pentobarbital (30 mg/kg) and maintained on artificial respiration.

Myocardial extraction after intravenous injection was determined in two dogs. Approximately 2 mCi of ^{42}KCl and $^{86}RbCl$ in 5–10 ml of saline were drawn

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up into separate syringes. Standards were prepared to determine the total injected dose in counts per min. The filled syringes were weighed and one-third of the dose was injected into two volumetric flasks that were then made up to 100 ml. Two to 3 ml of each standard was counted in a gamma well counter with the tissue samples. The syringe was reweighed and the remainder of the isotope was injected intravenously. The syringes were weighed again to determine the relative amount of isotope in the standard and injected dose.

The animals were sacrificed 2 min later. The heart and sections of muscle, liver, kidney, and lung were removed. The myocardium was cut into 1–2 gm sections. The positions of the sections in relation to the major vessels and chambers were mapped. The sections of myocardium and other organs were weighed and counted in a gamma well counter. The percentage of injected dose of ^{42}K and ^{86}Rb in the total myocardium and the percentage extraction per gram of myocardium for each tissue section was then calculated.

Total myocardial extraction as a percentage of injected dose was measured in seven dogs. A coronary catheter was introduced through the femoral artery into the left anterior descending artery. The position was confirmed by fluoroscopy and a small amount of contrast media (Renografin-76). After the preparation of a standard, 60 μCi of ^{42}K in 5 ml of saline was injected slowly over 2 min into five dogs. Absence of reflux of the isotope into the aorta was confirmed by injecting contrast at the same rate under fluoroscopic observation. In two dogs, the ^{42}K was injected at a faster rate (30 sec) to determine whether the rate of injection affected potassium extraction. Again, a lack of reflux was documented by observing the injection of contrast at the same rate as the radiopotassium under fluoroscopy. Simultaneous with ^{42}K injection, 2 mCi of ^{86}Rb was injected intravenously in two of the dogs. Two minutes after injection the animals were sacrificed. The myocardium was removed, sectioned, and counted as described above. Total myocardial extraction was calculated as a percent of injected dose. The first-circuit myocardial extraction (FCME) of ^{42}K was calculated from the formula

$$FCME = \frac{M - IV}{1 - IV}$$

where M represents the total myocardial extraction of ^{42}K and IV is the extraction of ^{86}Rb after intravenous injection.

The rate of potassium efflux was determined in one dog, and three dogs were imaged after the intracoronary injection of ^{43}K. A coronary catheter was positioned in the LAD artery under fluoroscopic control. The dog was placed in the left lateral projection and positioned under a gamma scintillation camera. Approximately 0.5 mCi of ^{43}KCl in 2 ml of saline was injected into the catheter and flushed with 4–5 ml of saline. Efflux was measured by monitoring the myocardial washout for 2 hr. Data were stored on magnetic tape continuously for the first 20 min and then for 2 min at 15-min intervals for 1½ hr. A digital printout of the myocardial washout was obtained by placing an electronic cursor over the myocardium. Counts were integrated over 30-sec intervals.

Imaging of the dogs was performed with the gamma camera using a high-energy, straight-bore (1,000-hole) collimator and a 25% window placed symmetrically over the 373-keV photopeak. Lateral, left and right anterior obliques and anterior views were obtained collecting 300,000 counts in 4–10 min for each view.

RESULTS

The total myocardial extraction of ^{42}K and ^{86}Rb after intravenous injection in two dogs was 4.7–5.7% of the injected dose. The ^{42}K and ^{86}Rb extractions were similar in each dog (Table 1). In the first dog, the total myocardial extraction was 5.6% for ^{42}K and 5.6% for ^{86}Rb. In the second dog, the ^{42}K extraction was 4.8% as compared to 4.7% for ^{86}Rb. Because of the similarity in the results, we used the myocardial distribution of ^{86}Rb after intravenous injection as a substitute for potassium.

After direct injection of ^{42}K into the left anterior descending artery, the myocardial extraction was

TABLE 1. TOTAL MYOCARDIAL EXTRACTION FOLLOWING INTRAVENOUS INJECTION

	(Percent of injected dose)	
Dog	^{42}K	^{86}Rb
1	5.7	5.7
2	4.8	4.7

Myocardial extraction following intracoronary injection of ^{42}K (Percent of injected dose)

Dog	^{42}K	^{86}Rb(IV)
3*	30.3	
4*	34.7	4.0
5*	42.7	
6*	31.3	
7*	35.2	6.0
mean	34.8	
8†	32.7	
9†	37.1	
mean	34.9	

* 2-min intracoronary injection.
† 30-sec intracoronary injection.

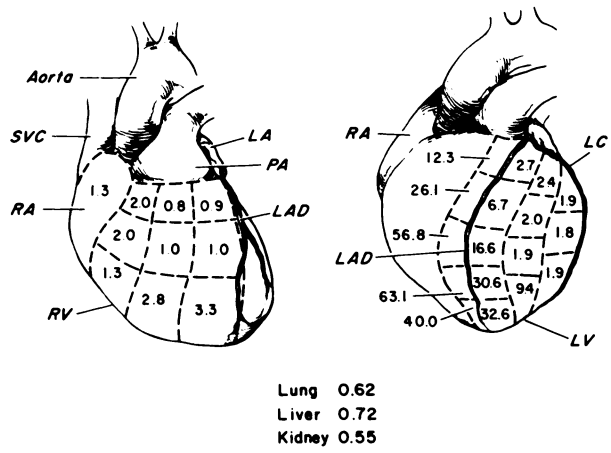

FIG. 1. Ratio of myocardial concentration after intracoronary (LAD) and intravenous injection of potassium analogs.

30–42% (Table 1). In two dogs, the first-circuit myocardial extraction (FCME) was calculated using the simultaneous intravenous injection of ^{86}Rb and the intracoronary injection of ^{42}K. The FCME was 31.1 and 40.3% or 2.7–4.1% less than the total myocardial extraction. The extraction of potassium by surrounding tissues after intracoronary injection was reduced by approximately 40% (Fig. 1). Extraction was not altered significantly by a more rapid injection of the isotope. Total myocardial extraction after 30-sec intracoronary injections was 37.1% and 32.7%, well within the range of extractions after 2-min injections.

By mapping the individual tissue sections, the distribution of perfusion of a single coronary artery (LAD) could be compared with the distribution of total myocardial blood flow measured after an intravenous injection.

In Fig. 1, the numbers in each tissue section represent the ratio of the percentage of myocardial extraction between an LAD injection and an intravenous injection. The ratio was quite high in the sections immediately adjacent to the LAD, indicating that the primary blood supply to that tissue was from the left anterior descending artery. However, only 1 or 2 cm away from the LAD, the concentration of ^{42}K fell precipitously.

The efflux from the myocardium after the intracoronary injection of potassium appeared monoexponential for the first 30 min, after which the rate of change diminished (Fig. 2). The half-time for the initial part of the washout was 30 min with a clearance constant of 0.0231 min^{-1}. Images obtained after the intracoronary injection (Fig. 3) indicated satisfactory myocardial imaging with a high target-to-background ratio and minimal activity in surrounding and overlying tissues.

DISCUSSION

Measurement of myocardial blood flow from the distribution of radiopotassium was first proposed by Saperstein (*1,2*) and later investigated by Donato, Bing, Love, and others (*3–8*). Carr, et al have attempted to diagnose myocardial infarction after the intravenous administration of ^{131}Cs, a radiopotassium analog (*9*). The images were of poor quality because of the unsatisfactory physical properties of the radionuclide. Recently, isotopes of potassium and its analogs with satisfactory physical properties for practical clinical investigation of regional myocardial blood flow have become available. Hurley, et al have imaged areas of infarction after intravenous injection of ^{43}K (*10*) and Yano, et al have done the same with ^{129}Cs (*11*).

Myocardial extraction of potassium analogs has been measured using a number of biological models. The differences between coronary sinus and arterial concentrations of an intravascular tracer and radiopotassium have been determined after bolus and continuous injections in an isolated heart model (*12*). The fractional extraction for ^{42}K was 0.69 ± 0.08; 69% of the ^{42}K was extracted in a single pass through the coronary circulation.

Myocardial extraction of potassium analogs has been measured in the intact dog by coronary sinus

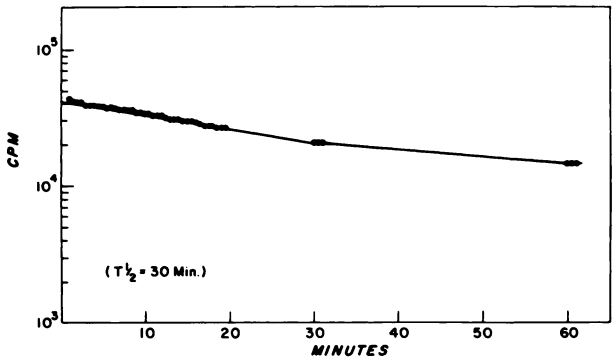

FIG. 2. Potassium-43 washout after intercoronary injection.

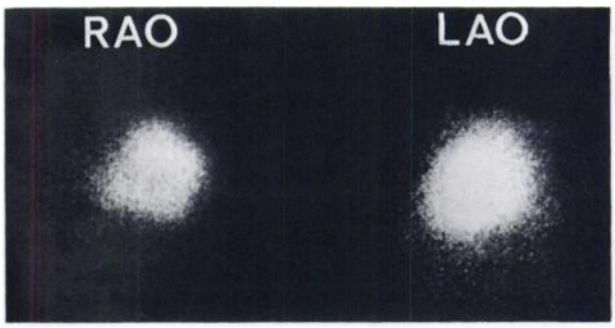

FIG. 3. Myocardial scintigraphs following intracoronary injection of ^{43}K. (A) Right anterior oblique, and (B) left anterior oblique.

sampling (*13*). A continuous intravenous injection of potassium analogs was monitored to maintain a plateau concentration of the isotopes in the venous blood. Extractions calculated from concentration differences between arterial and coronary sinus blood ranged from 71% for ^{42}K and 65% for ^{86}Rb to 22% for ^{131}Cs.

We determined the total and first-circuit myocardial extraction in dogs after the intracoronary artery injection of ^{42}K. Our results indicate a total myocardial extraction of 30–42%. The first-circuit myocardial extraction was 2.7–4.1% less than the total extraction. Potassium, which passes through the coronary vasculature on the first pass without extraction into the myocardium, was distributed proportionally to the cardiac output as if it had been injected intravenously.

There are a number of possible explanations for the discrepancy between our results and those reported previously. The efflux of ^{42}K from the myocardium appears multiexponential and has a very rapid component with a clearance of 0.65 ± 0.02 min^{-1} (*14*). This fast-flow component, thought to represent extracellular potassium efflux, would be completely washed out by the time the animal was sacrificed 4 min after beginning the injection. However, the total quantity of potassium in this compartment is less than 10% (*14*) and cannot by itself account for our low values.

A number of variables that could have affected extraction were carefully controlled. Before the radiopotassium was injected into the anterior descending artery, contrast was injected at the same rate under fluoroscopy to ensure that no contrast and therefore no radiopotassium refluxed into the aorta during injection. In addition, the ^{42}K was diluted to physiologic levels (3.2–5.6 mEq/liter) before injection. To determine whether the extraction was reduced due to tissue hypoxia resulting from obstruction of blood flow by the catheter, myocardial extraction in two dogs was measured after more rapid injections (30 sec) into the anterior descending artery, again after fluoroscopic confirmation that potassium was not refluxing into the aorta. The myocardial extractions were within the range obtained after prolonged injection (2 min) into the coronary circulation.

Therefore, the most compelling explanation is that the differences between the myocardial extraction we have found and those reported by others result from the effect of contrast on the potassium pump. Snyder, et al have shown a correlation between myocardial toxicity and sodium content in the contrast material (*15*). It seems likely that the contrast may well affect the sodium-active transport pump with a consequent effect on potassium extraction.

In any case, our purpose was to understand potassium extraction under conditions that simulate myocardial imaging in patients. This necessarily includes previous intracoronary injection of contrast agents and the injection of potassium analogs through coronary artery catheters. Under these conditions, 30–42% of the injected radiopotassium will be within the myocardium if imaging is begun several minutes after intracoronary injection compared with 5% following intravenous injection, a 6–8 fold increase in target organ concentration. In addition, the extraction in surrounding organs is reduced proportionately. The half-time for potassium efflux from the myocardium after intracoronary injection was 30 min, indicating a sufficiently slow washout to permit external imaging for some time after injection—assuming similar rate constants for dog and man.

Similar values for potassium efflux have been reported by others (*14,16*). The efflux appeared monoexponential for 30 min with a progressive tailoff after that time. It was not possible to determine whether this apparent decrease in clearance represented a buildup of ^{42}K in surrounding tissues or an efflux from several parallel myocardial compartments with substantially different rate constants. However, it is interesting to note that a multiexponential efflux has been observed from the isolated papillary muscle with rate constants very similar to ours (*14*). In any case, the efflux study indicates the feasibility of measuring the potassium efflux after intracoronary injection in the clinical setting.

Imaging with the gamma camera after intracoronary injection of ^{43}K resulted in myocardial scans with minimal extramyocardial background. Three-hundred thousand counts were acquired in 5–10 min, indicating that multiple projections can be obtained in a relatively short time after injection.

The mapping technique that we have described provides a unique model to study myocardial perfusion from a single coronary artery or branch of that artery. We compared the relative total myocardial perfusion from the left anterior descending artery. The ratio of LAD to total perfusion indicates that in the immediate vicinity of the artery, the LAD provides most or all of the tissue perfusion. However, within a short distance from the LAD, branches from other arteries, the left circumflex artery over the left ventricular wall, septal branches along the intraventricular septum, and the right coronary artery branches over the right ventricle provide substantial amounts of tissue perfusion. Thus, at least in the normal dog heart, a substantial amount of myo-

cardium appears to be supplied by more than one primary source.

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