Regional Myocardial Blood Flow Measured by I^{131} Labelled Macroaggregated Albumin (I^{131} -MAA)

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A method for the determination of regional myocardial blood flow in dog was reported. I^{131} labelled macroaggregated albumin was injected in left atrium and the radioactivity of regional myocardium was measured, which is proportional to the blood flow to that region.

The right ventricle and the left ventricle were loaded separately and the distribution of myocardial blood flow under these conditions was compared with that of unloaded heart.

RECENTLY radioisotopes have been applied for the study of coronary circulation in animals and man. Since Love and Burch¹⁾ reported a method to measure myocardial blood flow using Rb^{86} in 1954, this radioisotope was fully investigated and applied by many authors²⁾⁻⁷⁾ for the experimental and also for the clinical determination of myocardial blood flow.

Ross and his coworkers⁸⁾ reported a method to measure coronary blood flow in man using radioactive inert gases such as Kr^{85} or Xe^{133} . Though this method required selective injection of radioactive gas solution into the coronary artery, it enabled separate measurement of the right or left coronary arterial blood flow in man.

Experimental determination of regional myocardial blood flow has also become possible by the application of these isotopes in animals. Sapirstein⁴⁾ and Guzman et al.⁷⁾ used Rb^{86} for it in rats and dogs. Na^{24} and K^{42} were also applied in the same way. But these methods always have left some problem on extraction ratio of these isotopes between blood and myocardial tissue, which should be constant and independent from the blood flow. In 1961 MacLean and his coworkers⁹⁾ used Na^{24} glass microsphere instead of Rb^{86} or other radioisotopes. The extraction ratio of this substance was considered to be constant. But the specific gravity of this substance is greater than blood; consequently causing questionable mixture with blood.

Recently I^{131} macroaggregated albumin was developed by Taplin and his coworkers¹⁰⁾ and its usefulness for pulmonary scanning was demonstrated.¹¹⁾⁻¹⁴⁾ This substance is completely trapped by capillaries of the

organs; i.e. its distribution is proportional to regional blood flow. Besides, this has the same specific gravity as serum, which enables complete mixture of the substance with blood. Considering these advantages, we applied it for the measurement of regional myocardial blood flow in dog.

PRINCIPLE

The rate of accumulation of a substance in any region of the body is directly proportional to the blood flow to the region, provided that the substance is completely trapped in tissue capillaries and is not metabolized during the period of observation. I^{131} macroaggregated albumin is a particle ranging $20-60\mu$ in diameter and is completely trapped by capillaries through a single passage. If I^{131} macroaggregated albumin is injected into left atrium, it is carried by blood and distributes to each part of myocardium, thus the measurement of regional myocardial blood flow is possible.

METHOD

1) Preparation of I^{131} macroaggregated albumin. Macroaggregated albumin labelled with I^{131} was prepared by the improved method reported by us elsewhere.¹³⁾ In brief, this method is as follows. One percent solution of I^{131} labelled human serum albumin with high specific activity (1.5 mc./mg.) was acidified dialysing with acetic acid buffer solution to a final pH of 5.5. The material was then heated for 10 min. in 90°C oscillating at a frequency of 100 times per min. to get suspension of macroaggregated albumin labelled with I^{131} . The mean size of the particle prepared by this method is about $40-60\mu$ in diameter.

2) Experiment. Six mongrel dogs weighing 6 to 13 Kg. were anesthetized with intravenous injection of 30 mg./Kg. of pentobarbital sodium. Thoracotomy was performed using respirator, and polyethylene catheter was inserted in the left atrium into which $50\mu\text{c.}$ of I^{131} MAA was injected (control group).

In 3 dogs of the second group (group of right ventricular pressure loading), pulmonary embolism was produced by the injection of a large amount of non-labelled macroaggregated albumin into the femoral vein to produce right ventricular pressure loading, while the systemic blood pressure and pulmonary arterial pressure were recorded simultaneously through catheters inserted in the femoral artery and pulmonary artery. When pulmonary arterial pressure reached its plateau, then I^{131} MAA was injected into the left atrium by the same procedure as control group.

In 3 dogs of the third group (group of left ventricular pressure loading), descending aorta was ligated to produce left ventricular hypertension. Left ventricular pressure and femoral arterial pressure were recorded continuously through the catheters. When both pressures became stable, I^{131} -MAA was injected by the same route.

In all groups, 20 sec. after the injection of MAA into the left atrium, the heart was removed and washed in tapped water. After weighing it, 3 pieces of myo-

cardium ranging 0.1–0.3 Gm. in weight were cut out of the following part of the heart; right atrium, left atrium, interventricular septum, apex and conus of the right ventricle and posterior wall and apex of the left ventricle. Each piece of the myocardium was weighed and its radioactivity was counted in a well-type scintillation counter to calculate radioactivity per Gm. of the myocardium, which is designated as C_i . The rest of the heart was homogenized and the mean radio-activity of the total cardiac muscle per Gm. was calculated, which is designated as C_m . Ratio of C_i/C_m , which is considered to represent the relative myocardial blood flow, was calculated in each part of the heart and compared each other in both control group, the group of right ventricular pressure loading, and the group of left ventricular pressure loading.

RESULTS

The results of C_i/C_m calculated above are shown in Table I and Fig. 1. In normal dogs (No. 1–6), the C_i/C_m of posterior wall of the left ventricle was the largest. No significant difference was noted in the apex of the left

Fig. 1. Relative myocardial blood flow in normal dog.

C_i : cpm./Gm. of regional heart muscle

C_m : cpm./Gm. of total heart muscle

Ratio of C_i/C_m represents the relative regional myocardial blood flow.

Fig. 2. Autoradiogram of myocardium.

After 50 μ c. of MAA was injected in left atrium, the heart was removed and ventricular muscles were cut in horizontal plane. Each specimen was put on X-ray film and kept in dark refrigerated room for 6 days.

White spots represent particles of MAA distributed in myocardium.

ventricle, right ventricle and septum. Ci/Cm of the left and right atria were less than those of the ventricular myocardium. Autoradiography also confirmed these findings. (Fig. 2).

In the group of right ventricular pressure loading (No. 7-9), Ci/Cm of the right ventricular muscles was significantly greater than that of control

Fig. 3. Regional myocardial blood flow in right ventricular pressure loading.

C_i/C_m of RV conus and RV apex is significantly higher in this group than that of normal group.

group, which suggested the right ventricle received larger share of the total myocardial blood flow in right ventricular pressure loading (Table I, Fig. 3).

Pulse rate and pressures measured in pulmonary artery and femoral artery are shown in Table II. At the time of injection the pulmonary pressure was raised 6–20 mm.Hg and femoral arterial pressure was lowered about 20–30 mm.Hg than in control period.

In the group of left ventricular pressure loading (No. 10–12), C_i/C_m of the apex of the left ventricle was significantly greater than the control group, making a contrast to the group of right ventricular pressure loading (Table I, Fig. 4).

Fig. 4. Regional myocardial blood flow in left ventricular pressure loading.

C_i/C_m of LV apex is significantly higher in this group than that of normal group.

Table I

Control group							
No. of exp.	RA	LA	septum	RV conus	RV apex	LV p. wall	LV apex
No. 1	0.51	0.99	1.34	0.67	0.76	1.51	0.95
No. 2	0.36	0.83	1.15	0.94	0.88	1.32	1.05
No. 3	0.32	0.57	1.16	1.01	1.03	1.38	1.22
No. 4	0.41	—	0.81	1.18	0.63	1.12	0.61
No. 5	0.34	0.58	0.67	0.86	0.87	1.29	0.84
No. 6	0.48	0.86	0.87	1.25	0.69	2.19	1.24
Mean $\pm$ SD	0.40 $\pm$ 0.08	0.77 $\pm$ 0.19	1.00 $\pm$ 0.26	0.97 $\pm$ 0.21	0.81 $\pm$ 0.14	1.49 $\pm$ 0.38	0.99 $\pm$ 0.24
Group of RV pressure loading							
No. 7	0.95	1.65	1.16	1.76	1.86	1.23	0.89
No. 8	0.77	1.50	0.90	1.43	1.24	0.84	0.74
No. 9	0.20	0.20	1.60	1.68	0.88	1.45	0.89
Group of LV pressure loading							
No. 10	0.23	0.37	1.10	0.70	0.41	1.35	2.06
No. 11	0.37	0.47	1.37	0.86	0.71	1.29	1.36
No. 12	0.29	0.34	1.06	0.78	0.95	1.65	1.38

RA: right atrium

LA: left atrium

Septum: interventricular septum

RV conus: outflow tract of pulmonary artery of right ventricle

RV apex: anteroposterior wall of right ventricle

LV p. wall: posterior wall of left ventricle

LV apex: apex of left ventricle

Table II

No. of exp.	Control			After pulmonary embolism		
	HR	FA	PA(m) or RV	HR	FA	PA(m) or RV
No. 7	144	130/110	12	120	110/97	21
No. 8	138	150/110	26/0	144	162/115	50/0
No. 9	180	144/105	15	148	102/90	21

HR: Heart rate per min.

FA: Femoral arterial pressure (mm. Hg)

PA(m): mean pulmonary pressure (mm. Hg)

RV: right ventricular pressure (mm. Hg)

Table III

No. of exp.	Control		After aortic constriction	
	HR	Ao. Pr. (m)	HR	Ao. Pr. (m)
No. 10	114	100/60 (70)	114	126/104
No. 11	150	100/80 (88)	132	150/120
No. 12	192	142/100 (110)	174	160/128

Ao. Pr. (m): Aortic pressure (mean)

Pulse rate and pressures of this group are shown in Table III. At the time of injection of MAA, left ventricular systolic pressure was higher than the control period by 18–50 mm.Hg.

DISCUSSION

The method reported here is valid with assumptions that 1) the mixture of I^{131} MAA with blood is complete before its distribution to the myocardium, 2) all the MAA carried to the region are trapped by the capillaries, but do not significantly impede regional blood flow 3) the number of the particle of MAA is sufficiently large to overcome the statistical error. In this experiment I^{131} MAA was injected into the left atrium and MAA has almost the same specific gravity as blood. The first problem is resolved by these facts. As to the second problem, our previous report¹¹⁾ showed that MAA was large enough to be trapped by capillaries almost completely. And the standard deviation of the values of this experiment showed the statistical error is within permissible range.

One of the advantages of this method is that it has no problem on extraction ratio between blood and tissue and also no problem on time of measurement after the injection, which rubidium and potassium method has. But with this method only, the absolute value of the blood flow cannot be calculated, unless the cardiac output is measured simultaneously.

Sapirstein et al.¹⁾ reported in rats that the myocardial blood flow of the right ventricle is greater than that of the left, while Levy and Guzman et al. observed in dog the blood flow of the left ventricle and septum is greater than that of the right ventricle. Superiority of the right ventricle in blood flow in rats can probably be accounted for by the anatomical and functional difference in the pulmonary artery resulting different pulmonary resistance between dogs and rats. Our results showed the posterior wall of the left ventricle received the largest share of the myocardial blood flow and there was no significant difference among the rest of the ventricular muscles. The reason of this fact is obscure at the present time.

In the group of right ventricular pressure loading, the right ventricle received the greater share of the blood flow than the left ventricle. This fact agrees with the report by Guzman et al.⁷⁾

In contrast to this, in the group of left ventricular pressure loading, myocardial blood flow was greater in the left ventricular muscle than in the right ventricular one. More marked difference in myocardial blood flow between left and right ventricle might be attributable to an induced systolic pressure elevation in the former.

We believe this method can be applied further for the measurement of myocardial blood distribution in various conditions of the heart.

CONCLUSION

1) Regional myocardial blood flow was measured in dog using I^{131} labelled macroaggregated albumin.

2) In 6 normal dogs the regional myocardial blood was arranged as follows in order of quantities to the region. Posterior wall of the left ventricle > apex of the left ventricle, right ventricle and septum > left atrium > right atrium.

3) In 3 dogs, under right ventricular pressure loading the muscles of the right ventricle received larger share of the total myocardial blood flow than in normal dogs.

4) In 3 dogs under left ventricular pressure loading the apex of the left ventricle received larger share of the blood.

5) We believe this method can be applied further to the measurement of regional myocardial blood flow under various conditions of the heart.

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