Regional Myocardial Perfusion Rates in Patients with Coronary Artery Disease

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ABSTRACT Regional myocardial perfusion rates were estimated from the myocardial washout of ^{133}Xenon in 24 patients with heart disease whose coronary arteriograms were abnormal and 17 similar subjects whose coronary arteriograms were judged to be normal. Disappearance rates of ^{133}Xe from multiple areas of the heart were monitored externally with a multiple-crystal scintillation camera after the isotope had been injected into a coronary artery and local myocardial perfusion rates were calculated by the Kety formula.

The mean myocardial perfusion rates in the left ventricle exceeded those in the right ventricle or atrial regions in subjects without demonstrable coronary artery disease. In this group there was a significant lack of homogeneity of local perfusion rates in left ventricular myocardium; the mean coefficient of variation of left ventricular local perfusion rates was 15.8%.

In the patients with radiographically demonstrable coronary artery disease, a variety of myocardial perfusion patterns were observed. Local capillary blood flow rates were depressed throughout the myocardium of patients with diffuse coronary disease but were subnormal only in discrete myocardial regions of others with localized occlusive disease. Local myocardial perfusion rates were similar to those found in the group with normal coronary arteriograms in patients with slight degrees of coronary disease and in those areas of myocardium distal to marked coronary constrictions or occlusions which were well supplied by collateral vessels.

In subjects with right coronary disease, the mean right ventricular perfusion rates were significantly subnormal; in seven subjects of this group perfusion of the inferior left ventricle by a dominant right coronary artery was absent or depressed. The average mean left ventricular perfusion rate of 12 subjects with significant disease of two or more branches of the left coronary artery was significantly lower than that of the group with normal left coronary arteriograms. In the patients with abnormal left coronary arteriograms, the average coefficient of variation of local left ventricular perfusion rates was significantly increased (24.8%).

The studies provide evidence that coronary artery disease is associated with increased heterogeneity of local myocardial perfusion rates. They indicate that radiographically significant vascular pathology of the right or left coronary artery may be associated with significant reductions of myocardial capillary perfusion in the region supplied by the diseased vessel.

INTRODUCTION

A reasonable hypothesis concerning the pathogenesis of angina pectoris and of cardiac failure in patients with coronary atherosclerosis assumes that there are local reductions of myocardial blood flow in regions supplied by diseased blood vessels; these reductions in flow induce tissue hypoxia and impair myocardial contractility (1). Although this postulate is widely accepted there are few published data which directly support it. Indirect evidence has been provided by animal experiments in which reduction of the coronary blood supply to areas of left ventricle reduced myocardial oxygen consumption, reversed the normal myocardial extraction of lactate from arterial blood, and depressed ventricular function (2–4). Studies in patients with arteriographically demonstrable coronary lesions have shown increased extraction of oxygen from the coronary circulation (5), increased levels of lactate in coronary venous blood (6), and local

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abnormalities of ventricular wall contraction during induced angina pectoris (7).

Measurements of myocardial blood flow in patients with coronary artery disease have been ambiguous. Both normal and reduced rates of nutrient flow per gram tissue were found by investigators who externally monitored myocardial extraction of a tracer or analyzed single inert gas wash-out curves from heart muscle with precordial detectors or by coronary sinus sampling (8–11). Studies using H_2 provided evidence that myocardial blood flow was more heterogeneous than normal in coronary patients (12); however regional flow reductions were not quantitated in these studies. The observations of two groups that the rate constants of washout of radioactive tracers injected directly into different areas of myocardium were reduced in patients with coronary artery disease (13, 14) have not been confirmed largely because the technique necessitates thoracotomy and because loss of tracer or hyperemia at the injection site cannot be excluded.

In a previous report, a technique to estimate capillary perfusion in multiple areas of the myocardium with ^{133}Xenon and a multiple-crystal scintillation camera was described (15). This communication presents results of studies of regional myocardial perfusion measured by the new technique in 24 patients with arteriographically demonstrated coronary artery lesions. A statistical analysis of the results obtained in the group with diseased coronary vessels is compared with a similar analysis of the myocardial perfusion patterns obtained in 17 patients with arteriographically normal coronary arteries.

METHODS

41 patients were studied in the diagnostic cardiovascular laboratory at the Roosevelt Hospital, New York. In each patient, a history and a complete physical examination was performed along with routine blood studies and urinalysis, chest X-ray, and electrocardiogram. All were seen by the cardiac consultation service and cardiac catheterization was performed only on patients in whom the study was clinically indicated. Patients were studied because of angina pectoris, atypical cardiac pain, or congestive heart failure of unclear etiology. During right and left heart cardiac catheterization, coronary arteriograms were obtained by the technique of Sones (16), and the myocardial perfusion study was performed with ^{133}Xe and a multiple-crystal scintillation camera using the technique described previously (15). The nature of the coronary blood flow study using ^{133}Xenon was explained to each subject and informed consent was obtained. There were no complications resulting from the study in any of the patients.

Statistical analysis. The results of the studies were analyzed by standard statistical techniques (17). The results were declared significant if P was < 0.05.

The studies were divided into four groups (see Table II) based upon the interpretation of the coronary cinearteriogram. The groups were: (*a*) "normal" left coronary studies, (*b*) "normal" right coronary artery studies, (*c*) "abnormal" left coronary artery studies and (*d*) "abnormal" right coronary artery studies. The data for each study presented include: the mean blood flow rate recorded by crystals overlying the appropriate cardiac region, the standard deviation of the observations, and the number of crystals from which the mean value was calculated. In studies of the left coronary artery the coefficient of variation was calculated. Estimates of the mean perfusion rates in regions of left ventricle supplied by the anterior descending, diagonal, and circumflex branches were computed by averaging the perfusion rates in crystals which were crossed by each arterial branch on the myocardial perfusion pattern (15).

The standard deviation of the flow measurement recorded by each individual crystal (SDM) was calculated (i.e., the within-crystal SD); the mean SDM for crystals overlying the myocardium in each study is presented in Table II. These estimates of the average accuracy of the blood flow measurements obtained in each study must be distinguished from the standard deviation of the blood flow rates observed for the whole ventricle in a given study (i.e., the between-crystal SD) since the latter term includes not only measurement error but also area to area variations in local perfusion rates.

Table III contains a summary of the data in the four groups of studies. The numbers presented were obtained by calculating the mean and standard deviation of the mean data from the individual studies listed in Table II.

Several different comparisons were made: (*a*) The left ventricular and left atrial perfusion rates were compared in the left coronary studies by an analysis of variance; in the right coronary studies, the left ventricular, right ventricular and right atrial flows were similarly compared. The mean left ventricular perfusion rate found by left coronary artery isotope injections was compared with the mean right ventricular perfusion rate measured after right coronary injection by a "*t*" test.

(*b*) Significant differences in the estimates of blood flow in regions of the myocardium supplied by the left anterior descending, left diagonal, and left circumflex in patients with "normal" left coronary arteries were sought by an analysis of variance. A similar analysis was not carried out on patients with diseased left coronary arteries because localization of the artery of origin of reduced capillary perfusion in myocardial regions distal to narrowed or occluded coronary vessels was frequently impossible.

(*c*) The between-crystal standard deviation of the local myocardial blood flow rates recorded over the whole ventricle (SD) was compared with the measurement error (SDM) by a χ^2 test in each study to test whether the variability of local flow rates over the whole ventricle is greater than expected from measurement error alone, i.e., whether there is true heterogeneity of local myocardial flow rates.

(*d*) The significance of the difference in mean ventricular blood flow rate between patients with normal and abnormal arteriograms was tested by a t test for both the right and left coronary artery studies.

(*e*) The significance of the difference in the coefficient of variation of left ventricular myocardial flow rates between patients with normal and abnormal coronary arteriograms was tested by techniques used to determine the variance of the ratio of two independent, normally distributed random variables, i.e., by a Taylors' series expansion in which the higher order terms are ignored.

RESULTS

Table I lists the clinical and hemodynamic evidence of heart disease in each patient. Table II presents the re-

TABLE I

Clinical and

Study No.	Patient		Diagnosis	Historical features			ECG
	Age	Sex		Angina	MI	Other	
Normal left coronary artery studies							
7	51	F	PMD	+	0	dyspnea	Abn. ST-T
16	53	F	IHSS, MR	+	0	syncope	LVH
19	51	M	PMD	+	0	0	N
20	56	F	RHD, MS, AI	0	0	systemic embolus	Abn. ST-T, AF
21	57	M	PMD	+	0	CHF	Abn. ST-T, AF
3	67	M	AS	0	0	syncope	2° AV Block, RBBB
6	58	M	PMD	0	0	CHF	Abn. ST-T
30	51	F	RHD, MS	0	0	dyspnea	Abn. ST-T, AF
36	45	F	RHD, AS, MR	0	0	CHF	Abn. ST-T, RAD
Abnormal left coronary artery studies							
8	59	M	ASHD	0	++	CHF	1° AV Block
9	41	M	ASHD	+	+	0	ASMI
14	40	M	ASHD	+	+	0	AMI
17	51	F	ASHD	+	++	0	ASMI
22	39	M	ASHD	0	+	CHF	IMI
23	45	M	ASHD	+	0	0	N
25	41	M	ASHD	+	0	0	Abn. ST-T
27	70	M	ASHD	+	++	CHF	1° AV Block, IMI
28	78	F	ASHD	+	+	syncope	LVH
10	56	M	ASHD	+	+	CHF	IMI
33	52	M	ASHD	+	++	0	AMI

Clinical and hemodynamic data on the patients. All of the studies have been classified into four groups according to the radiographic interpretation of the coronary arteriogram and the coronary artery into which ^{133}Xe was injected to measure myocardial perfusion. The abbreviations used are: (*a*) For diagnosis: AI, aortic insufficiency; AS, aortic stenosis; ASD, atrial septal defect; ASHD, arteriosclerotic heart disease; IHSS, idiopathic hypertrophic subaortic stenosis; MR, mitral regurgitation; MS, mitral stenosis; PMD, primary myocardial disease; RHD, rheumatic heart disease; (*b*) for historical features; CHF, congestive

(*Table I—*

Hemodynamic Data

Heart size	LV Ventriculogram	HR	BP	LVP	RVP	CI
		beats/min	*mm Hg*	*mm Hg*	*mm Hg*	*liters/min per m²*
Enlg.	LV hypertrophy	70	140/70	140/12	40/8	3.1
Enlg.	subvalvular obstruction	90	120/70	200/14	30/2	3.0
N	N	98	135/70	135/13	25/8	3.7
N	Abn. mitral valve motion	70	140/70	140/25	45/6	2.2
Enlg	Diminished LV contraction	108	140/80	140/25	45/6	1.6
Enlg.	—	84	130/70	170/15	32/6	4.0
Enlg.	Increased EDV	66	180/90	180/26	18/4	2.4
N	MR	90	130/80	130/8	36/4	2.1
Enlg.	MR	70	110/55	175/14	65/12	3.3
Enlg.	Enlg. LV, MR	75	110/70	110/40	85/20	1.9
N	N	80	100/60	100/12	20/8	2.9
N	Inf. Lat. Aneurysm	96	120/80	120/12	32/8	4.5
Enlg.	Ant. Lat. Aneurysm	85	160/80	160/12	30/6	2.7
Enlg.	Akinetic Inf. wall, MR	88	100/60	100/18	30/6	3.3
N	N	85	140/80	140/8	24/6	3.1
N	Akinesis Inf. wall	66	140/80	140/16	20/8	3.5
Enlg.	Enlg. LV, MR, Apical Aneurysm	90	100/60	100/25	16/6	2.0
Enlg.	Enlg. LV, AI, MR	60	170/60	170/4	27/8	2.0
Enlg.	Enlg. LV, Akinesis Inf. wall	90	108/55	108/18	26/8	2.9
Enlg.	Ant. Aneurysm	60	120/10	120/30	28/8	2.0

heart failure; MI, myocardial infarction; (*c*) for electrocardiogram; Abn. ST-T, abnormal ST-T segment changes; AF, atrial fibrillation; AMI, anterior myocardial infarction; ASMI, anteroseptal myocardial infarction; AV Block, 1° and 2° atrioventricular block; IMI, inferior myocardial infarction; LVH, left ventricular hypertrophy; N, normal; RHD, rheumatic heart disease; RBBB, right bundle branch block; LV, left ventricle; HR, heart rate; BP, blood pressure; LVP, left ventricular pressure; RVP, right ventricular pressure; CI, cardiac index (liters/min per m²).

continued)

(TABLE I—

Study No.	Patient		Diagnosis	Historical features			ECG
	Age	Sex		Angina	MI	Other	
38	67	M	ASHD	+	+	syncope	1° AV Block, LVH
39	57	M	ASHD	+	+	CHF	AMI
40	54	M	ASHD	0	+	CHF	AMI
41	41	M	ASHD	0	+	0	Abn. ST-T
42	58	M	ASHD	+	++	0	Inf. and AMI
Normal right coronary artery studies							
4	67	M	RHD, AS	0	0	CHF	LVH
5	66	M	PMD, AI	0	0	CHF	LVH
7	51	F	PMD	0	0	dyspnea	Abn. ST-T
15	61	M	RHD, MR, AI	0	0	CHF	LVH
20	56	F	RHD, MS, AI	0	0	systemic emboli	Abn. ST-T, AF
32	60	F	AS, RHD	0	0	syncope	LVH
34	48	M	PMD	+	0	0	N
35	59	M	RHD, MR	0	0	CHF	Abn. ST-T, AF
Abnormal right coronary artery studies							
2	52	M	ASHD	+	++	0	IMI
8	59	M	ASHD	0	++	CHF	1° AV Block, Abn. ST-T
9	41	M	ASHD	+	+	0	ASMI
10	56	M	ASHD	+	+	CHF	IMI
12	40	M	ASHD	+	+	0	Abn. ST-T
13	48	M	ASHD	+	+	CHF	IMI
18	62	M	ASHD	+	+	CHF	AMI
29	61	M	ASHD	0	+	CHF	AMI

gional myocardial perfusion data obtained in each study and the interpretation of the arteriogram obtained at the time of measurement of blood flow. Table III presents a summary of the data for each of four groups of patients.

Normal left coronary artery studies. Individual myocardial perfusion studies in three patients (5, 16, 36) have been presented (15). The mean myocardial blood flow of the left ventricle of 64.1 ml/100 g·min (Table II) was significantly greater than the mean left atrial flow of 41.5 ml/100 g·min. The mean coefficient of variation of local left ventricular blood flow rates was 15.8% and did not change significantly with position (16.3% for AP vs. 15.2% for LAO). Significant inhomogeneity of flow was present in the left ventricular myocardium,

concluded)

Heart size	LV Ventriculogram	HR	BP	LVP	RVP	CI
		beats/min	*mm Hg*	*mm Hg*	*mm Hg*	*liters/min per m²*
Enlg.	Enlg. LV, MR	72	130/70	130/16	85/12	1.4
Enlg.	Enlg. CV, MR	84	155/90	155/23	40/6	2.6
Enlg.	Ant. Lat. Aneurysm	110	95/55	95/30	45/11	2.4
N	N	85	160/90	160/13	18/6	3.6
Enlg.	Generalized Hypokinesis	71	120/65	120/21	26/7	2.2
Enlg.	MR, AI	85	120/80	160/30	48/10	1.9
Enlg.	AI	95	200/85	200/38	75/14	3.3
Enlg.	LV hypertrophy	70	140/70	140/12	40/8	3.1
Enlg.	AI, MR	80	125/80	125/6	24/2	2.3
N	Abn. mitral valve motion, AI	70	140/70	140/8	35/6	2.2
Enlg.	—	52	80/60	230/24	30/7	—
N	N	66	110/70	110/8	18/6	2.4
Enlg.	MR	90	190/90	190/13	50/8	2.6
N	Inf. wall Dyskinesis	65	120/70	120/11	20/8	3.9
Enlg.	Enlg. LV, MR	75	110/70	110/40	85/20	1.9
N	N	80	100/60	100/12	20/8	2.9
Enlg.	Enlg. LV, Akinesis Inf. wall	90	108/55	108/18	26/8	2.9
N	N	70	120/75	120/11	26/6	2.5
Enlg.	Decr. contraction, Inf. wall	55	190/100	190/11	22/7	2.3
Enlg.	Ant. lat. Aneurysm	76	110/60	110/35	55/12	2.3
Enlg.	Ant. Aneurysm, MR	90	160/110	160/18	—	1.5

since the between-crystal variance of flows significantly exceeded the variance of the flow measurements in all nine patients (see statistical analysis). In only one patient in this group (7, Table II) was a significant difference found between the mean perfusion rates in regions of the left ventricle supplied by the three main branches of the left coronary

Normal right coronary artery studies. The mean myocardial perfusion rate of the right ventricle of patients in this group was 47.8 ml/100 g·min and was significantly different from the flow of 64.1 ml/100 g·min found in "normal" left coronary studies. Furthermore, in the seven patients in whom a dominant right coronary artery allowed the comparison, the inferior left ventricu-

TABLE II

Myocardial Perfusion Data and

	Left atrial region			Left ventricle				
	No. of crystals	F*	SD*	No. of crystals	F*	SD*	CV	SDM*
Normal left coronary artery studies								
A-P position								
7	7	34.4	7.2	35	62.3	10.5	16.9	6.1
16 (1)	11	57.3	15.4	36	93.0	16.2	17.4	5.8
(2)	11	69.1	7.4	36	86.1	12.3	14.3	5.9
19	6	51.8	6.5	32	55.3	10.2	18.5	5.1
20	—	—	—	25	55.2	8.2	14.9	5.8
21	4	46.0	9.1	27	57.4	7.9	13.8	6.0
LAO position								
3	—	—	—	35	55.7	9.1	16.3	6.2
6 (1)	3	28.3	1.2	39	50.7	8.5	16.8	5.7
(2)	4	29.8	5.7	37	42.5	5.7	12.8	5.7
30 (1)	3	45.0	5.3	38	79.2	14.2	17.9	7.4
(2)	—	—	—	38	70.3	12.3	17.5	6.6
36 (1)	1	29.4	—	33	68.4	6.6	9.7	5.5
(2)	1	30.5	—	33	69.5	9.5	13.7	6.0
Abnormal left coronary artery studies								
A-P position								
8	4	29.0	3.4	35	39.1	5.3	13.7	5.7
9	8	32.6	10.1	32	46.7	16.3	34.9	7.3
14	10	47.7	10.7	33	60.8	18.4	30.3	8.1
17	11	44.8	11.4	27	46.3	8.6	18.5	6.9
22	7	43.6	7.5	42	57.4	7.4	12.9	6.4
23	—	—	—	38	69.1	12.6	18.2	7.8
25	11	41.5	7.5	30	57.9	16.1	27.8	12.0
27	8	43.1	12.2	37	53.0	8.8	16.6	8.4
28	10	57.3	10.8	37	68.8	9.9	14.3	6.8
LAO position								
10	4	45.8	5.7	40	33.9	12.6	37.2	6.1

* In ml/100 g·min.

Myocardial perfusion data and the results of coronary arteriography. The abbreviations used are: No. of crystals, the number of crystals overlying the stated region of the heart; F, mean flow rate in ml/100 g·min obtained by averaging the flow obtained from all crystals overlying the region; SD, the between-crystal standard deviation of the flows (ml/100 g·min), calculated from the variance of F; CV, coefficient of variation computed as SD/F × 100; SDM, the mean standard deviation of the flow measurements in ml/100 g·min; this is obtained by averaging the variances of each individual flow rate from all crystals overlying the ventricle (it is an estimate of measurement accuracy); LAD, left coronary artery, anterior descending branch; LD, left coronary, diagonal branch; LC, left coronary, circumflex branch; RCA, right coronary artery. The arteriograms were coded as follows: 0, normal vessels; 1, abnormal vessels, insignificant disease; A, vessel irregularity; B, narrowing <50%, no slowing of flow, no collaterals; 2, abnormal vessels, significant disease; A, narrowing <50% with segments 1 cm long, slowing of flow or

(*Table II*—

Interpretations of the Coronary Arteriograms

Left ventricular regional flow estimates*			Interpretation of arteriograms				
LAD	LD	LC	LAD	LD	LC	RCA	Comments
71.4	63.9	56.6	0	0	0	0	
94.3	98.0	84.3	0	0	0	0	
55.1	59.3	54.5	0	0	0	0	
56.9	54.9	52.3	0	0	0	0	
54.7	61.8	57.3	0	0	0	0	
60.0	52.1	53.1	0	0	0	0	
45.6	56.2	51.0	0	0	0	0	
79.9	82.8	78.8	0	0	0	0	
68.4	66.7	68.5	0	0	0	0	
38.7	35.4	42.6	2C	1A	2A	2C	Collaterals bridging AD obstruction
48.0	54.7	41.8	2C	2A	2C	0	Collaterals from RCA to LAD and LC
58.8	75.4	53.2	2C	2B	2D	0	Collaterals to LC from RCA and LAD
49.2	45.4	44.5	2D	2B	2C	1B	Collaterals around obstruction of LC and to LAD from RCA and LC
55.9	58.3	59.8	1A	1A	1B	2D	
71.1	—	65.5	1A	0	2D	0	Collaterals from LD to area distal to occluded branch of LC
59.7	61.0	46.8	1B	1B	1B	2D	
49.3	55.0	54.9	2B	2C	2C	2D	Collaterals to LC from RCA
71.1	71.0	66.0	2B	2B	2B	2C	
28.3	38.4	37.8	2B	2A	2A	2D	Collaterals from RCA to area distal to occlusion of LC and to LAD

collaterals; B, narrowing 50–80%; C, narrowing >80%; D, occlusion.

In order to estimate the average perfusion rate in different regions of the myocardium, the computer printout of local myocardial flow rates was superimposed upon a tracing of the patient's coronary arteriogram as previously described (15). Flows from crystals whose area on the perfusion pattern was touched by the tracing of each of the three major branches of the left coronary artery were averaged to obtain an estimate of the mean perfusion rates in ventricular regions supplied by each of these branches. In studies of the right coronary artery (see Figs. 9, 17, 19; reference 15) crystals which were located to the left of the main right coronary artery on the perfusion pattern were estimated to overlie right atrial tissue. Crystals on the pattern which were located to the right and cephalad of the main right coronary artery down to the crux of the posterior descending branch were regarded as overlying right ventricular tissue; crystals along the posterior descending arterial branches to the right of the crux of the artery were regarded as overlying the inferior-apical left ventricle.

continued)

(TABLE II—

	Right atrial region			Right ventricle				
	No. of crystals	F*	SD*	No. of crystals	F*	SD*	CV	SDM*
33	—	—	—	25	28.4	9.7	34.2	8.0
38	4	32.0	9.7	50	41.2	10.4	25.2	6.2
39	3	69.7	11.8	38	93.9	16.0	17.1	6.8
40	7	78.3	17.0	51	58.5	26.8	45.8	9.7
41	2	56.0	2.8	32	58.4	10.9	18.7	9.2
42	5	45.0	11.6	40	41.3	12.9	31.2	6.8
Normal right coronary artery studies								
LAO position								
4	5	25.0	4.1	19	40.2	8.9	6.8	
5	14	39.4	8.2	13	61.1	9.0	6.9	
7	5	25.0	4.7	10	41.9	9.4	6.0	
15	6	28.2	3.8	11	57.7	7.9	8.3	
20	5	29.2	7.2	9	40.6	12.8	7.8	
32	6	56.2	8.1	12	58.3	14.2	9.8	
34	7	35.1	7.3	11	51.9	11.8	9.8	
35	5	31.0	8.7	21	31.0	6.7	6.1	
Abnormal right coronary artery studies								
LAO position								
2	5	32.6	9.1	21	41.4	16.2	7.9	
8	8	37.4	13.7	23	38.5	8.9	6.3	
9	11	22.5	6.1	15	36.9	9.5	6.6	
10	8	40.3	11.9	14	32.2	8.4	6.2	
12	5	36.4	11.1	7	30.0	8.0	7.0	
13	8	27.5	7.8	24	28.1	8.5	6.8	
18	3	35.7	21.1	14	40.2	6.9	7.9	
29	6	42.2	6.5	22	33.5	7.8	6.8	

lar flow (69.0 ml/100 g·min) was significantly greater than right ventricular flow (52.5 ml/100 g·min). Mean right atrial perfusion of 33.6 ml/100 g·min was significantly lower than that of the right ventricle.

Abnormal left coronary artery studies. In 12 of the 16 patients there was significant occlusive abnormality of two or more left coronary branches. The mean left ventricular perfusion rate of 48.0 ml/100 g·min in this group was significantly less than mean left ventricular flow found in patients with "normal" left coronary arteriograms (Table III). In the remaining four patients with minor disease or occlusion of one branch, the mean left

concluded)

Left ventricle			Interpretation of arteriograms				
LAD	LD	LC	LAD	LD	LC	RCA	Comments
22.9	32.5	29.0	2C	2B	2B	2D	Multiple collaterals bridging LAD and LC obstructions and to RCA
38.4	45.3	47.6	2C	2B	2B	2D	Collaterals from LC to RCA
80.3	100.9	93.0	2C	1A	1B	1A	
32.7	74.5	77.8	2D	0	1B	0	Some vessel distortion by anteriolateral aneurysm
60.6	55.7	57.5	2B	2A	2C	2D	Collaterals bridge R coronary obstruction
32.7	39.0	50.8	2C	2D	0	2D	LC and LAD collaterals to R coronary
7	51.4	18.8	0	0	0	0	
18	83.9	11.1	0	0	0	0	
10	72.5	10.1	0	0	0	0	
12	83.2	9.2	0	0	0	0	
9	52.1	6.7	0	0	0	0	
6	69.3	19.0	0	0	0	0	
12	70.9	9.0	0	0	0	0	
—	—	—	1A	0	0	0	Nondominant RCA,
0	0		2D	2C	0	0	Occlusion of posterior descending branch of RCA, fibrosis of inferior LV at operation
0	0		2C	2B	2A	1A	>90% obstruction of posterior descending branch of RCA. Collateral bridging proximal RCA obstruction
9	43.4	5.4	0	2C	2C	1B	Collaterals from RCA to LC
0			2D	2B	1B	1B	Collaterals supply RV but not inferior LV
10	39.4	5.9	2B	2B	2C	2B	
0			2D	2B	1B	2B	Collaterals bridging obstruction to supply RV but not inferior LV
5	39.4	8.4	2B	2D	2B	2B	
0			2D	2B	2B	2B	Collaterals bridging R coronary obstruction; supply RV but not LV

ventricular blood flow was not subnormal. 13 of the 16 patients showed significant heterogeneity of left ventricular flow (part (*c*) of *statistical analysis*); the remaining 3 had diffuse lesions of two or three major left coronary branches. The mean coefficient of variation of local left ventricular flows (25.2%) in the 16 patients with abnormal left coronary arteriograms was significantly greater than the 15.8% observed in those with radiographically normal left coronary arteries.

Abnormal right coronary artery studies. The mean right ventricular perfusion rate in eight patients with abnormal right coronary arteriograms was 35.1 ml/100

TABLE III

Summary of Results in Four Groups of Patients

Arteriograms	Left atrial region		Left ventricle		Coeff. of var.
	No. of crystals	Flow*	No. of crystals	Flow*	
		ml/100 g·min		*ml/100 g·min*	
Normal left (9 patients)	4	41.5 ±13.7	33	64.1 ±13.9	15.8
Abnormal left (disease of two branches 12 patients)	7	43.2 ±9.2	35	48.0 ±12.0	25.2

	Right atrial region		Right ventricle		Left ventricle	
	No. of crystals	Flow*	No. of crystals	Flow*	No. of crystals	Flow*
		ml/100 g·min		*ml/100 g·min*		*ml/100 g·min*
Normal right (8 patients)	6	33.6 ±10.3	13	47.8 ±10.9	11	69.0 ±13.1 (n = 7)
Abnormal right (8 patients)	7	34.3 ±6.6	18	35.1 ±4.9	8	40.7 ±2.3 (n = 3)

* Mean flow ± SD of the observation.

The Table summarizes results obtained in patients with normal and abnormal right and left coronary arteriograms. Mean perfusion data obtained in three cardiac regions in individual studies have been averaged for each group of patients.

g·min, a value significantly lower than the right ventricular flow of 47.8 ml/100 g·min observed in patients with normal right coronary vessels. Mean atrial perfusion rates were comparable in the two groups. Only three of seven patients with obstructive lesions of a dominant right coronary exhibited left ventricular perfusion after right coronary isotope injection. In these three the mean left ventricular myocardial flow of 40.7 ml/100 g·min was significantly lower than the 64.0 ml/100 g·min seen in similar studies of patients with a nonobstructed dominant right coronary.

Regional myocardial perfusion. The patterns of local myocardial perfusion rates varied widely in the 18 patients with coronary artery disease. Figs. 1–8 show selected studies.

Slight to moderate alterations in coronary vessel caliber did not affect myocardial capillary blood flow rates in four subjects. Fig. 1 depicts the myocardial perfusion pattern obtained in a patient (Table II, 22) in whom < 50% narrowing of the branches of the left coronary was associated with a mean left ventricular blood flow rate of 57 ml/100 g·min and a 13% coefficient of variation; both values are comparable with findings in subjects without demonstrable coronary vascular disease (Table III). Myocardial perfusion rates in the regions of the right atrium and right ventricle were also not significantly below normal in two subjects with minor degrees of right coronary artery disease (12 and 18 of Table II).

Local myocardial perfusion rates were significantly and diffusely depressed throughout the left ventricle of seven patients with advanced coronary atherosclerosis involving all three branches of the left coronary artery (Table II, 9, 10, 17, 27, 33, 38). Fig. 2 illustrates the perfusion pattern in one of these studies (33); total occlusion of the anterior descending plus diffuse disease of a diagonal and circumflex branches of the left coronary artery in the patient were associated with diffusely subnormal rates of myocardial capillary perfusion (mean LV perfusion = 28 ml/100 g·min). Subnormal perfusion of right ventricular myocardium distal to an occlusion of the right coronary artery is illustrated by study 13, Fig. 3; similar results were observed in three other studies (Table II, 10, 12, 29).

12 of 24 patients with arteriographically abnormal coronary arteries demonstrated reductions of regional myocardial perfusion which could be correlated to radiographic lesions of the coronary vessels (Table II, RCA: 2, 8, 10, 13, 18, 24; LCA: 9, 10, 14, 33, 39, 40). Fig. 4 demonstrates the perfusion pattern observed after left coronary ^{133}Xe injection in study 9 (A. P.); the patient had sustained an anterior descending occlusion and also

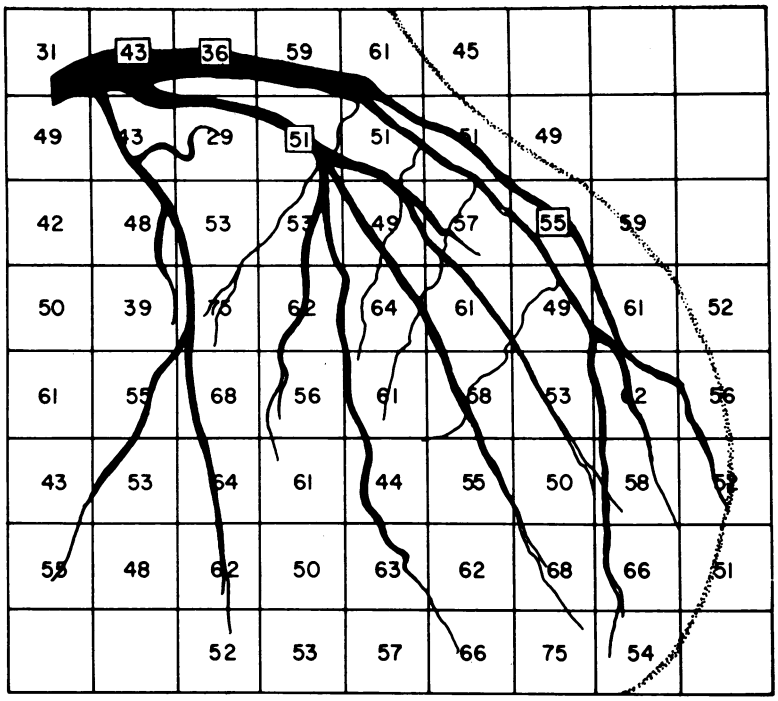

FIGURE 1 The computer printout showing the myocardial blood flow rates in different regions of the heart has been magnified, aligned, and superimposed upon a tracing of the patient's left coronary arteriogram (study 22, A-P view). The area recorded by each crystal is indicated by the rectangle enclosing the number which in this and subsequent figures expresses the local myocardial blood flow rate in ml/100 g · min. The mean left ventricular perfusion rate and the coefficient of variation of local flow rates found in this patient with minor degrees of diffuse coronary vascular disease were within the range observed in subjects with completely normal left coronary arteriograms.

had an occlusion of the midportion of the circumflex artery. The isotope study revealed that local tissue perfusion rates were reduced in the myocardial regions distal to the occluded circumflex artery and in the regions supplied by the terminal portions of the anterior descending. The absence of evidence of capillary perfusion in the inferior left ventricular myocardium after ^{133}Xe injection into a dominant right coronary was observed in five patients (Table II); examples appear in Figs. 3 and 5.

Fibrosis and aneurysm. The coronary arteriogram in study 2 (Fig. 5) revealed total occlusion of the main right coronary artery, collateral bridging of the obstruction, and a distal total obstruction of the posterior descending branch. Isotope did not penetrate to the inferior surface of the left ventricle where ventriculography indicated an akinetic area which at operation was found to be an area of fibrosis distal to the occluded branch of the right coronary. Similarly, ^{133}Xe did not penetrate extensively into a large anterolateral left ventricular aneurysm of patient 40 (Fig. 6).

Collateral blood flow. Restoration or maintenance of myocardial perfusion by collateral blood vessels was documented in eight studies (Table II, left: 8, 17, 23; right: 2, 8, 9, 13, 29). Figs. 3 and 5 illustrate collateral bridging of an occluded right coronary artery with maintenance of right ventricular perfusion via flow through these collaterals.

The right coronary arteriogram in study 9 (Fig. 7) indicated the presence of collateral vessels extending from the posterior descending branch of the right coronary artery to the posterior inferior wall of the left ventricle; the perfusion study indicated that the nutrient circulation of this region of the left ventricle was partially maintained by these collateral vessels (Fig. 13 of reference 15). The myocardial perfusion pattern after left coronary injection in this same patient appeared in Fig. 4.

A fourth example of collateral blood flow appears in Fig. 8; ^{133}Xe was injected into an internal mammary artery 1 yr after it had been implanted into the left ventricle of a patient with a > 90% occlusion of the an-

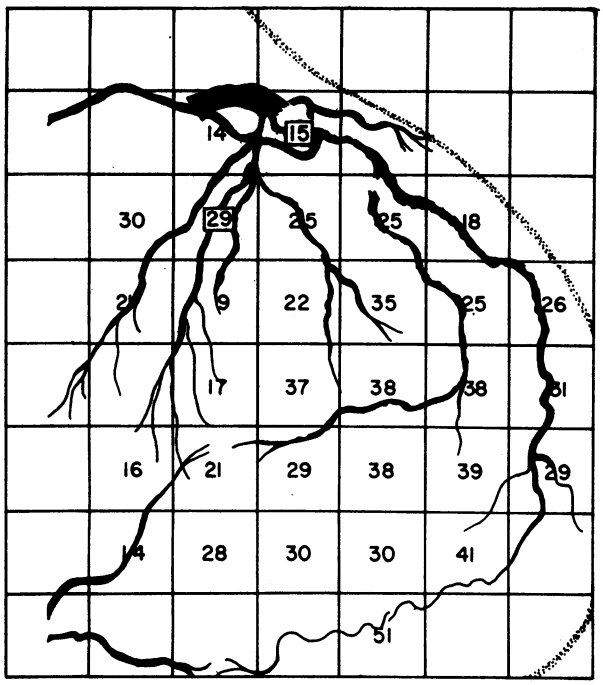

FIGURE 2 Perfusion rates throughout the left ventricle were strikingly reduced in study 33 of a patient with marked disease of the diagonal and circumflex branches and complete occlusion of the anterior descending branch of the left coronary artery (LAO projection).

terior descending artery. The capillary perfusion rates in the region of the anterior left ventricle supplied by the implanted vessel were within the normal range.

DISCUSSION

In the present studies capillary perfusion in multiple regions of the human heart was estimated by monitoring the wash-out curves of ^{133}Xe simultaneously from many areas of myocardium with a multiple-crystal scintillation camera after the indicator had been injected into the coronary circulation with a catheter.

The theoretical basis and the assumptions of the method employed in these studies have been discussed previously (15), along with technical details, mathematical treatment of the data, and the advantages and limitations of the technique.

Three observations in 17 patients with cardiac disease but normal coronary arteriograms provide evidence that local myocardial capillary blood flow rates are not homogeneous in hearts free from demonstrable coronary atherosclerosis: (*a*) Mean myocardial perfusion rates differed significantly in left ventricle, right ventricle and atrial regions, (*b*) the mean coefficient of variation of local left ventricular flow rates was 15.8%, (*c*) statistical analysis indicated that the local myocardial perfusion rates in left ventricle were truly inhomogeneous; the crystal-to-crystal variations in flow were not due solely to chance or to random errors of measurement.

The values obtained for the mean ^{133}Xe clearance rate and for the average capillary blood flow rate in the left and right ventricular myocardium are very similar to those reported for patients with normal coronary arteries by investigators who measured single myocardial wash-out curves of ^{133}Xe (8, 18), ^{85}Kr (9), and H_2 (12). The finding of considerable heterogeneity of local myocardial capillary blood flow rates in human hearts without radiographically demonstrable coronary artery disease is also consistent with previous studies which employed different measurement techniques. Brandi found that local ^{133}Xe clearances, measured after direct intramyocardial injection, varied 18% in the dog (19). Sullivan, Taylor, Elliott, and Gorlin, using a similar technique, found that local ^{85}Kr clearance constants varied 19% in four dogs and in two patients without coronary disease (14). Considerable variations in the myocardial blood flow rates in various regions of left or right ventricle were also apparent in the data of Domenech et al. (20) who studied the distribution of coronary blood flow in dogs with the radioactive

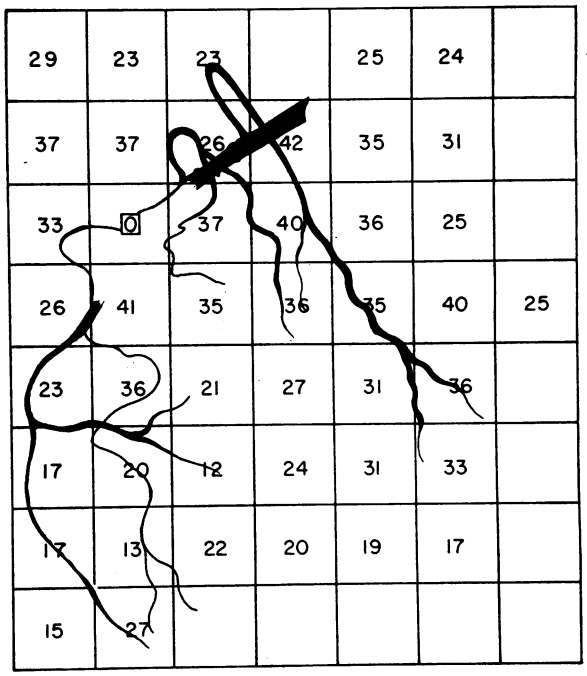

FIGURE 3 Subnormal right ventricular perfusion rates are apparent in this study (13) of a patient with occlusion of the main right coronary artery. After ^{133}Xe was injected into this dominant vessel, significant amounts of radioactivity were not recorded by scintillation crystals overlying the inferior left ventricle.

microsphere technique. Differences in the myocardial perfusion rates of subendocardial and subepicardial layers of normal dog ventricular muscle which have been reported by some (21), but not all observers (22), cannot be accurately assessed with the technique employed in the present studies (15).

To our knowledge, the present studies of the patterns of regional myocardial perfusion in 24 patients with abnormal coronary arteriograms are the first to be reported in intact subjects. In interpreting the results in patients with coronary artery disease it is important to reiterate, however, that the possibility of local diffusion barriers to passage of inert gas or local alterations of the tissue/blood partition coefficient for ^{133}Xenon by areas of fibrosis or ischemia cannot be completely excluded. The precautions which were taken to minimize possible effects of in vivo alterations of λ in different regions of the heart have been discussed previously **(15).**

The data reveal that coronary atherosclerosis may be associated with a wide spectrum of myocardial perfusion patterns. Local myocardial perfusion rates in patients with minimal coronary vascular disease and in regions of the heart which were well supplied with collateral vessels were comparable with values found in patients with normal coronary arteriograms. Diffuse reductions in myocardial perfusion were found throughout the ventricles of patients with arteriographic occlusive disease of many coronary arterial branches; and localized reductions of myocardial perfusion were observed in patients with discrete coronary vascular lesions.

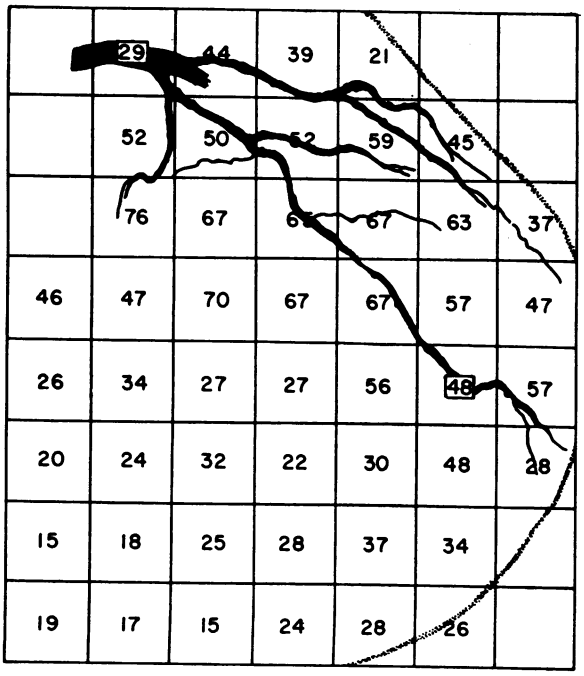

FIGURE 4 This study (9, A-P projection) demonstrates reduced tissue perfusion in the region of myocardium normally supplied by the occluded circumflex branch of the left coronary.

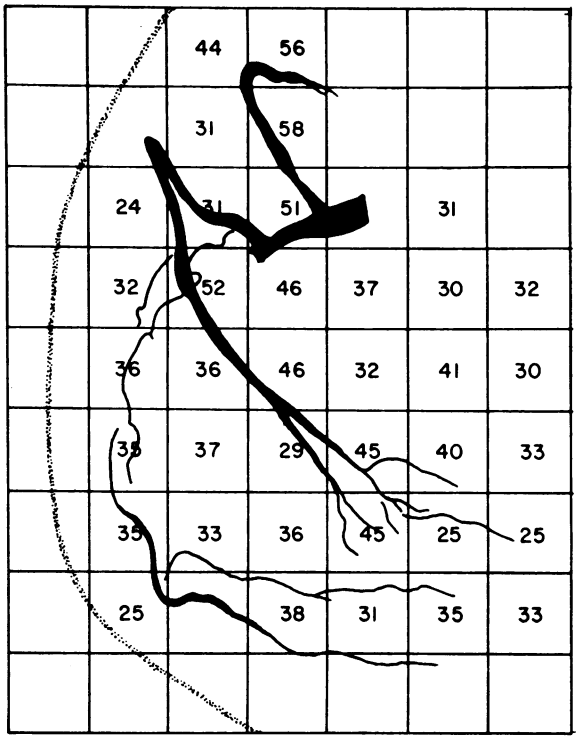

FIGURE 5 The perfusion pattern observed in the patient (study 2) illustrates that normal rates of myocardial perfusion can be maintained in right ventricle by collateral vessels which arise proximal to a major right coronary occlusion. Whereas maintenance of perfusion by collateral vessels is apparent in right ventricle, there is no detectable perfusion in the region of left ventricle normally supplied by this dominant right coronary vessel.

The finding that: (*a*) regions of diminished myocardial perfusion could be localized to specific arteriographic lesions in 12 of the 24 patients and (*b*) the mean coefficient of variation of local left ventricular blood flow rates was greater among patients with occlusive left coronary disease than in those with normal left coronary arteriograms, indicate that heterogeneity of local myocardial perfusion rates is significantly increased by radiographically demonstrable coronary artery disease. These results confirm and extend observations of other investigators. Sullivan et al. (14) found that myocardial clearance constants of ^{85}Kr (direct injection technique) were less uniform in 29 coronary patients than in 4 normal subjects. Klocke et al. (12) provided indirect evidence for nonuniformity of myocardial perfusion in coronary disease by demonstrating that H_2 myocardial wash-out curves (coronary

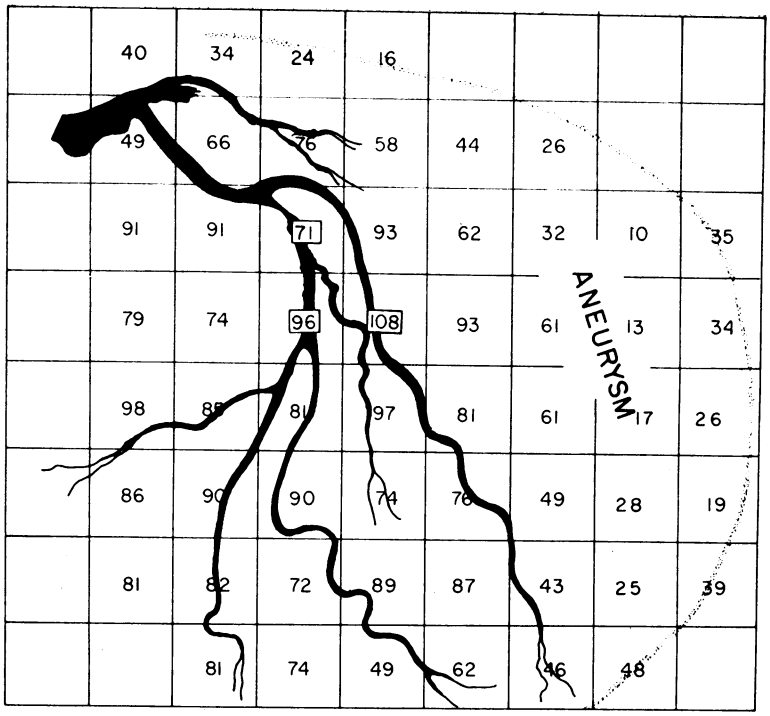

FIGURE 6 ^{133}Xe was injected into the main left coronary artery of patient 40 12 wk after an acute anterior myocardial infarction. The arteriogram and perfusion pattern (A-P projection) revealed that tissue perfusion was normal in left ventricular regions supplied by the diagonal and circumflex branches of the left coronary. Isotope penetrated poorly and washed out slowly from the large aneurysm formed distal to the total occlusion of the anterior descending branch.

sinus sampling) deviated from a single exponential in dogs with experimental coronary occlusion and in patients with abnormal coronary arteriograms.

The mean left ventricular myocardial blood flow was reduced in 12 patients with significant arteriographic abnormalities of two or more left coronary branches. Mean right ventricular perfusion was subnormal in eight patients with occlusive disease of the right coronary artery; and in seven with a dominant vessel, the normal supply to the inferior left ventricular myocardium was either absent or reduced. These reductions of the mean myocardial capillary blood flow in the left or right ventricle may contribute to the abnormalities of cardiac hemodynamics which are frequently observed in patients with coronary disease (Table I).[1]

[1] In the 25 subjects on whom left coronary artery studies were performed there was a significant correlation between the mean left ventricular perfusion rate and one hemodynamic index which has been related to myocardium oxygen consumption, i.e., the product of left ventricular systolic pressure and heart rate ($r = 0.642$, $P < 0.01$). There was no correlation between mean LV perfusion and heart rate ($r = 0.2151$), mean arterial blood presure ($r = 0.0310$), or cardiac index ($r = 0.0509$).

In subjects with severe disease of two or more branches of the left coronary there was not a clearly apparent correlation between our radiographic assessment of vessel caliber and the mean myocardial perfusion rate. This observation is compatible with a hypothesis (23) that atherosclerosis of small coronary radicles (not radiographically visible) may reduce myocardial capillary blood flow in patients with extensive large vessel disease. Findings of reductions of capillary perfusion distal to $>75\%$ narrowing of the left coronary in many of the patients with recurrent chest pains (e.g., 9, 38, Table II) lends support to the hypothesis that reductions of myocardial blood flow relative to metabolic need may be implicated in angina pectoris (24).

Five of the studies (e.g. Figs. 3, 5, 7) provided evidence: (*a*) that collateral blood flow can be measured with the new technique, and (*b*) that in some patients collateral blood vessels may maintain relatively normal capillary perfusion in regions of the heart beyond major arterial constrictions or occlusions. The infrequent history of right ventricular infarction in patients with extensive right coronary occlusive disease

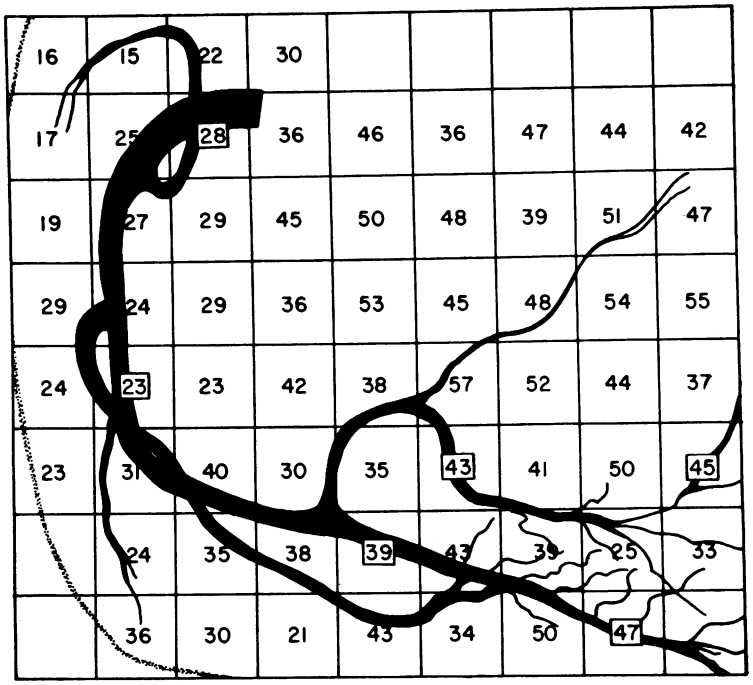

FIGURE 7 Abundant collateral vessels extend from a right coronary, which has no demonstrable disease, toward the posterior inferior left ventricle. The perfusion pattern obtained in this patient, whose left coronary study appears in Fig. 6, indicates that a significant portion of the nutrient blood supply of the inferior portion of the left ventricle was derived from these right coronary collaterals.

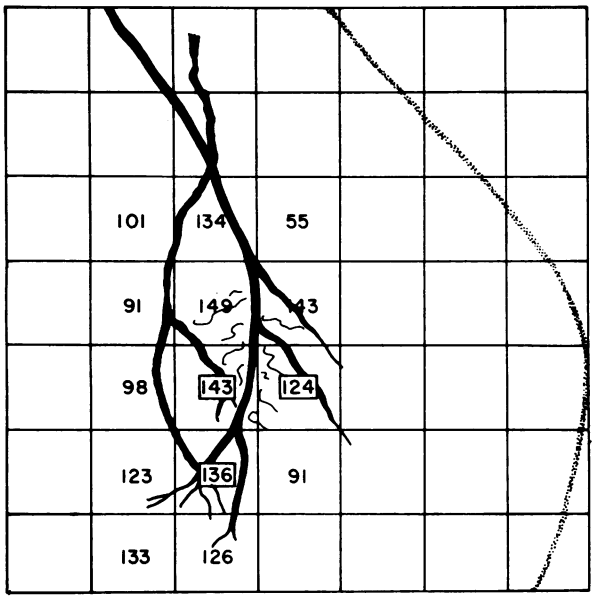

FIGURE 8 In this study of patient G, both contrast material and subsequently ^{133}Xe were injected into the origin of the internal mammary artery implant. The anterior descending artery with a > 90% occlusion at its origin filled in retrograde fashion via collateral vessels. The isotope study indicated that the capillaries of a significant segment of the anterior left ventricle were supplied by the implanted vessel.

(Tables I and II) may possibly be related to the frequency with which extensive intracoronary collaterals are observed in this region, and also to the lower oxygen requirements of the right ventricle (25).

The perfusion pattern obtained after ^{133}Xe was injected down the internal mammary implant of patient G (Fig. 8) indicates that the capillary network in ischemic myocardium of certain patients may be provided with a nutrient blood supply by this surgical procedure; an estimate of the amount of tissue supplied by the implant is obtained by totaling the areas viewed by crystals from which ^{133}Xe wash-out curves were obtained. Currently, the practical usefulness of the ^{133}Xe myocardial perfusion pattern as an aid in the preoperative diagnosis and selection of patients for coronary artery surgery and in the evaluation of surgical graft by-pass operations is under investigation.

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