Myocardial Blood Flow in Man: Effects of Coronary Collateral Circulation and Coronary Artery Bypass Surgery

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ABSTRACT The effects of coronary artery bypass graft (CAB) and coronary collaterals (CC) on myocardial blood flow (MBF) were studied in 24 patients undergoing 29 CAB's. MBF after CAB was compared to preexisting MBF by intraoperatively injecting ^{133}xenon via distal CAB with proximal CAB first occluded then open. Pressure gradients across bypassed obstructions were measured. The results were correlated with preoperative coronary arteriograms to determine the effects of CC on MBF and postobstructive perfusion pressures. Mean MBF was increased by CAB from 32±6 (SE) ml/min per 100 g (CAB occluded) to 118±13 ml/min per 100 g (CAB open). The ^{133}Xe clearance curves with CAB open were resolved into slow (19±2 ml/min per 100 g) and rapid (133±12 ml/min per 100 g) phases, suggesting that MBF remained heterogeneous after CAB. Vessels with less than 80% stenosis by angiography had pressure gradients less than 20 mm Hg across obstructions, high postobstructive perfusion pressures (75±7 mm Hg), and normal MBF (87±6 ml/min per 100 g) even with CAB occluded. Vessels with greater than 80% stenosis or total occlusion by angiography had significant pressure gradients with marked reduction of postobstructive MBF. No significant difference in postobstructive MBF was found when vessels with CC (21±4 ml/min per 100 g) were compared to those without CC (17±4 ml/min per 100 g) ($P > 0.4$).

These studies demonstrate that (*a*) mean MBF increased 268% after CAB, (*b*) heterogeneous MBF persisted after CAB, (*c*) CC were not associated with significant increases in MBF, and (*d*) vessels with less than 80% stenosis had less than 20 mm Hg gradient with minimal effect on resting MBF.

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INTRODUCTION

Coronary artery bypass surgery provides a unique opportunity to study in man the hemodynamics and flow patterns of the diseased coronary artery. Previous experimental investigations (1, 2) have demonstrated in canine hearts the alterations in coronary hemodynamics which follow acute and chronic coronary arterial constriction. These studies indicate the collateral circulation is capable of restoring flow to normal distal to coronary arterial obstructions. Recent clinical observations in man (3–7) are in conflict with the experimental studies, however, and suggest that coronary collateral flow provides an inadequate response to myocardial ischemia. Implicit in the concept of coronary bypass surgery is the capability of restoring flow to a myocardium rendered ischemic by coronary arterial obstruction. To justify a surgical approach, the improvement in myocardial flow resulting from bypass graft should significantly exceed that provided by collateral circulation.

The present study was designed (*a*) to measure the relative improvement in myocardial blood flow (MBF)[1] after coronary bypass graft, and (*b*) to correlate the preexisting MBF with the presence of collaterals and degree of coronary artery disease.

METHODS

Patient population. 24 patients (21 male, 3 female) ranging in age from 33 to 68 yr (mean age 48 yr) underwent coronary artery bypass procedure using saphenous vein grafts. A total of 29 coronary arterial obstructions were bypassed and evaluated in this study. 10 grafts were placed on right coronary arteries, 15 to left anterior descending coronary arteries, and 4 to left circumflex coronary arteries. With the exception of four patients (A. M., C. B., H. C., and J. R.), all operations involved single bypass grafts.

[1] *Abbreviations used in this paper:* CAB, coronary artery bypass graft; CC, coronary collaterals; MBF, myocardial blood flow.

Intraoperative determination of myocardial blood flow and pressure. Aorta to coronary artery bypass operations were performed under morphine anesthesia using saphenous vein grafts. Total cardiopulmonary bypass with induced ventricular fibrillation and hypothermia to 28–30°C was employed during the period of graft anastomosis. Measurement of coronary arterial pressure and blood flow was performed intraoperatively under stable hemodynamic conditions 20–30 min after terminating cardiopulmonary bypass, at normal temperatures, and in normal sinus rhythm. For the vessels studied in this series, the mean aortic pressure at time of flow measurements ranged from 62 to 100 and averaged 79±11 (SD) mm Hg. A small polyethylene catheter PE No. 160 was introduced into the distal saphenous vein bypass graft (Fig. 1) near its anastomosis to the distal coronary artery. The preexisting MBF determinations were made with the graft cross clamped proximally. ^{133}Xe (0.5 ml., 1.1 mCi) was injected into the distal saphenous vein bypass graft via the PE No. 160 tubing and flushed into the distal coronary artery with 3 ml normal saline solution. A shielded scintillation probe with 1-inch sodium iodide crystal was positioned approximately 10 cm above the myocardium perfused by the distal coronary artery. Counts were recorded with an analog, linear ratemeter (Picker Labmeter I, Picker Corp., Cleveland, Ohio) set at a time constant of either 0.1 or 0.3 sec, connected to a Picker 2990 rectilinear strip chart recorder. After a period of 40–60 sec the clamp was removed from the proximal bypass graft permitting the myocardium to be perfused by flow through the coronary artery bypass graft in addition to the preexisting flow from collaterals or antegrade across the coronary arterial stenosis. Precordial counting with the graft open was continued for 2½–3 min. In this manner, myocardial blood flows in the region supplied by the distal coronary artery were obtained with the graft open and occluded, thus permitting comparison of MBF before and after bypass graft. The sequence of occlusion and patency of the graft was randomized. Repeat injections were made with the graft open or occluded at 5-min intervals in several patients to document reproducibility of the method. In one patient not reported herein who underwent subsequent cardiac catheterization postoperatively, the ^{133}Xe clearance curves obtained by direct injection into the bypass graft were comparable to the intraoperative measurements obtained with the bypass graft open (110 vs. 113 ml/min per 100 g, respectively). These findings suggest the clearance rates obtained intraoperatively are similar to those which exist during life apart from effects of anesthesia and a previous period of extracorporeal support of the circulation. In seven patients direct injections (0.1 ml ^{133}Xe in saline) were made through a 25 gauge needle into epicardial fat to determine the washout pattern and $t_{\frac{1}{2}}$ for lipid tissue.

Myocardial blood flows were calculated from the formula $F = (K \cdot \lambda \cdot w)/P$ in which the clearance constant $K = 0.6931/$ half time in minutes, λ = myocardium-to-blood partition coefficient for ^{133}Xe (0.7) (8), $w = 100$ g, the actual weight of myocardium being unknown, but by convention flow is expressed per 100 g of tissue, and $P = 1.05$, the estimated specific gravity of myocardium (8–10). As discussed in the results, the majority of washout curves were best resolved into two exponential components (11) on the basis of a semilogarithmic plot.

Perfusion pressure in the distal coronary artery was determined via manometer connected directly to the PE tubing (Fig. 1). Pressures were obtained (*a*) during clamp occlusion of the proximal coronary bypass graft and (*b*) with graft open. The pressures obtained with graft open (effective central artery pressure) were compared to radial artery mean

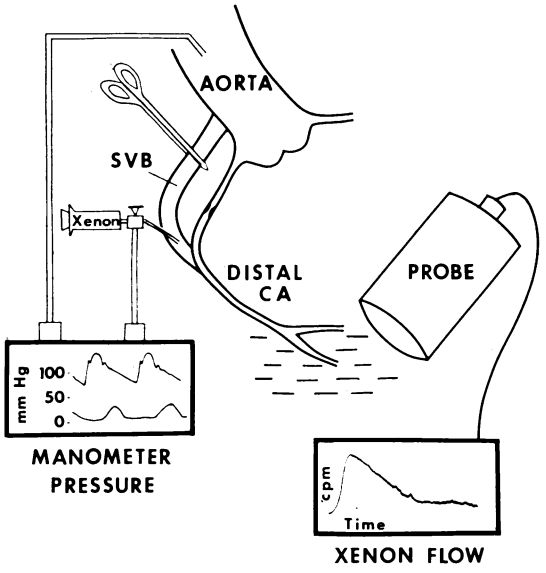

FIGURE 1 Schematic to demonstrate method for measuring intraoperative ^{133}Xe flow and pressures.

pressure. The pressure gradient across a given coronary arterial obstruction was determined by cross clamping the bypass graft proximally and simultaneously measuring pressure in the radial artery and distal bypass graft.

Analysis of coronary arteriograms. Selective coronary arteriograms were performed preoperatively on each patient within 3 wk of the operative procedure utilizing 9–6 inch General Electric (General Electric Company, Schenectady, N. Y.) or Siemens (Siemens Corp., Iselin, N. J.) 10–5 inch biplane image intensifier and recording on 16 mm film at 60 or 75 frames per sec, respectively. All patients had films of excellent radiographic quality. The arteriograms in both right and left anterior oblique projections were evaluated independently by three observers to determine the site and degree of coronary obstructions.

The per cent obstruction was calculated from the ratio of the smallest diameter of vessel visible at the lesion in either projection to the diameter of normal vessel immediately adjacent to the lesion in the same projection. The films were reviewed carefully to detect the presence of collateral vessels, and if present, the collaterals were classified anatomically as either epicardial or intramyocardial in origin. The time, in milliseconds, for the coronary artery distal to an obstruction to opacify after injection of contrast agent was measured using a projector-linked frame counter, taking the frame immediately preceding appearance of contrast agent at the origin of the coronary artery as t_o, and the first frame demonstrating opacification distal to the obstruction as the end point. This value, termed arteriographic appearance time, was calculated at least three times for each obstruction to document reproducibility of the method (within 30 msec). In those vessels with both antegrade and collateral filling of coronary artery beyond an obstruction, the distal coronary arterial filling times were calculated for both antegrade and collateral sources of filling. The distinction between antegrade and collateral filling times was made from separate injections of contrast agent first into the affected artery and then into the donor artery giving rise to the collateral vessel. Fig. 2 demonstrates schematically the filling of contrast agent in vessel distal to a subtotal obstruction where early appearance

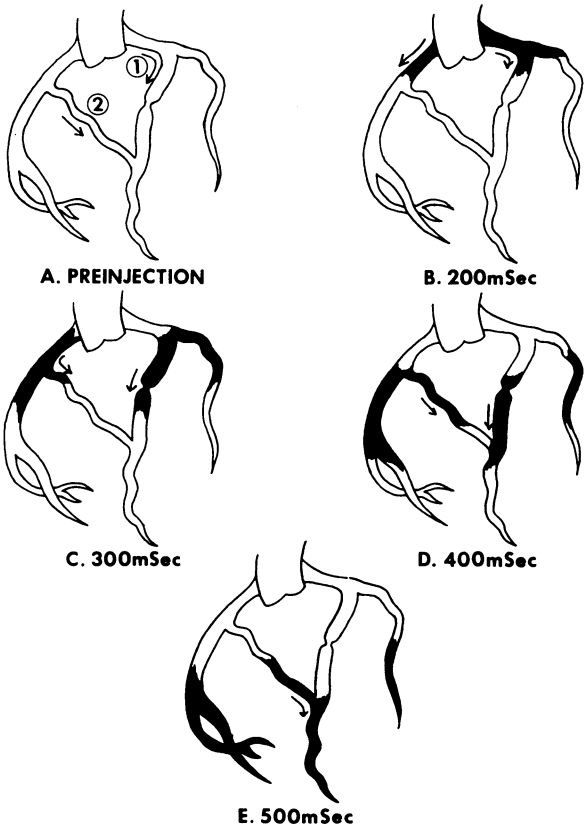

FIGURE 2 Angiographic recognition of variable coronary arterial transit times. The filling of contrast agent in a vessel distal to a subtotal obstruction may occur directly by antegrade flow from the proximal vessel (C) or slightly later from collateral flow (D).

is associated with antegrade flow (Fig. 2C) and slightly longer appearance time with collateral flow (Fig. 2D).

The vessels receiving bypass grafts were classified angiographically (Fig. 3) as follows: group A, vessels with less than 80% obstruction and no collaterals; group B, those with greater than 80% obstruction and no collaterals; group C, those with greater than 80% obstruction and collaterals; and group D, those with total obstruction and distal vessel filled by collaterals only.

RESULTS

The results of preoperative arteriographic analyses and corresponding intraoperative determinations of pressure and flow for the 29 vessels bypassed are summarized in Table I. The vessels are listed by arteriographic groups based on degree of obstruction and presence or absence of collaterals (Fig. 3). Intraoperative pressures were not measured in three patients (C. B., D. P., and W. B.), and flow rates were not measured with the graft clamped in two patients (J. R. and R. B.).

Effect of bypass graft on myocardial blood flow. For the total series, mean MBF with bypass graft clamped was 32±6 (SEM) ml/min per 100 g and increased to

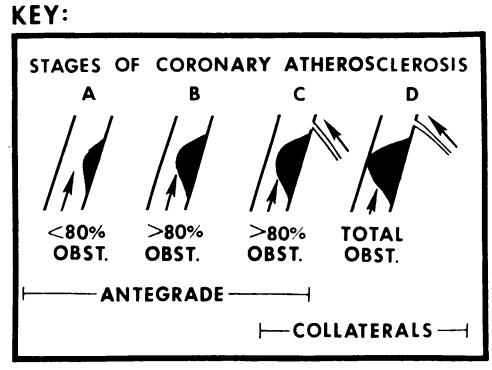

FIGURE 3 Arteriographic stages of atherosclerosis based on per cent obstruction and presence or absence of collaterals.

118±13 ml/min per 100 g with the graft open (Fig. 4). This represented a 268% mean increase in MBF for the total series after saphenous vein bypass graft. The level of myocardial flow was not systematically influenced by the artery receiving the graft or its site of attachment (Table I). Of interest were several vessels in which only minimal improvement in flow occurred (Fig. 4). With three exceptions (E. M., J. S., and H. W.), these were all vessels from group A in which preexisting flow and pressure beyond the obstruction was near normal with the graft clamped.

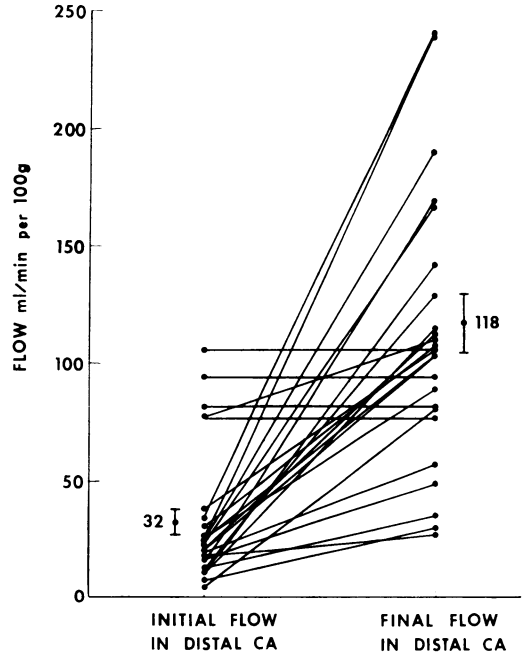

FIGURE 4 ^{133}Xe myocardial blood flow determinations with bypass graft closed (initial flow) and open (final flow). Mean values ±SE are shown for the group of initial and final flows.

TABLE I

Results of Preoperative Arteriography and Intraoperative Pressure-Flow Determinations

Patient	Arteriography			Graft clamped		Pressure gradient	Graft open flow	
	Vessel*	Dye appearance time		Flow	Pressure		Fast	Slow
		Ante‡	Collat§					
		msec		*ml/min per 100 g*	*mm Hg*	*mm Hg*	*ml/min per 100 g*	
Group A								
C. B.	RCA	217		78	100	0	110	16
L. B.	LAD	16		106	66	17	106	13
J. R.	RCA	150		N.M.‖	70	0	83	7
J. S.	LAD	16		94	72	0	94	8
M. C.	LCF	240		82	90	0	82	13
M. R.	LAD	16		76	50	20	76	13
Group B								
A. M.	LAD	350		4	32	44	81	14
E. Y.	LAD	267		23	50	22	113	15
E. M.	LAD	66		18	10	56	27	—
B. H.	RCA	283		13	13	65	287	14
R. B.	LAD	283		N.M.	26	47	124	37
C. B.	LCF	350		25	N.M.	N.M.	103	17
Group C								
J. S.	RCA	333	1347	7	30	54	30	—
J. C.	LAD	1333	2040	33	19	74	240	42
M. C.	RCA	1160	2000	24	30	68	238	32
R. D.	RCA	1173	1093	20	34	55	114	23
D. P.	LAD	627	733	10	N.M.	N.M.	170	19
H. W.	LAD	693	5520	12	30	60	35	—
H. C.	LAD	567	3100	25	21	61	167	26
C. D.	LAD	1067	1800	26	30	53	89	21
A. M.	RCA	1033	1817	16	15	47	128	19
Group D								
N. G.	LAD		2027	10	20	50	114	8
R. S.	LAD		1167	21	38	24	57	—
C. B.	RCA		1467	38	N.M.	N.M.	106	32
W. B.	RCA		1617	30	N.M.	N.M.	106	16
H. C.	LCF		2283	11	22	60	143	15
J. R.	LAD		2717	17	34	34	49	—
S. B.	RCA		1517	23	21	63	190	13
R. B.	LCF		1250	N.M.	33	43	48	—

* RCA, right coronary artery; LAD, left anterior descending coronary artery; LCF, left circumflex coronary artery.

‡ Ante, antegrade source of coronary opacification.

§ Collat, collateral source of coronary opacification.

‖ N.M., not measured.

Fig. 5 summarizes the intraoperative evaluation in a patient (H. D., Table I, group C) with severe obstruction to the left anterior descending coronary artery. Distal coronary pressure (Fig. 5, lower left panel) rose from a mean of 21 mm Hg with graft clamped to 82 mm Hg with graft open. The calculated pressure gradient across the coronary arterial obstruction was 61 mm Hg. A large increase in the precordial clearance of ^{133}Xe was observed with the graft open (Fig. 5, upper right panel). The calculated MBF from exponential plot (Fig. 5, lower right panel) revealed a preexisting MBF (graft clamped) of 25 ml/min per 100 g. With augmented flow after opening the bypass graft, the ^{133}Xe clearance was expressed as a double exponential with a rapid phase

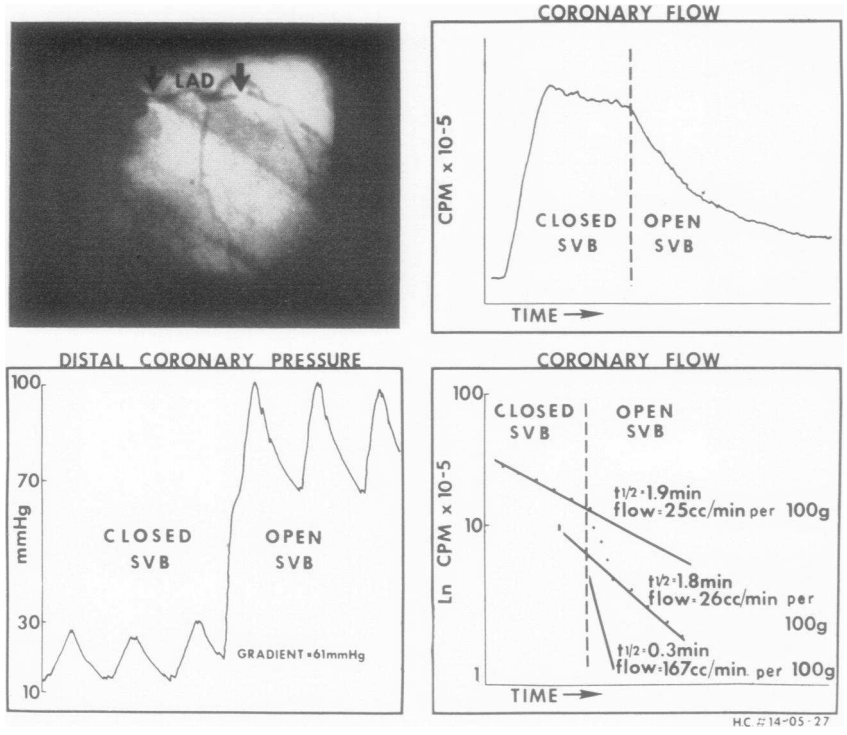

FIGURE 5 Results of arteriogram and intraoperative pressure and ^{133}Xe flow measurements for coronary artery with severe obstruction. SVB, saphenous vein bypass.

of 167 ml/min per 100 g and a slow phase of 26 ml/min per 100 g. In a majority of patients, the clearance of ^{133}Xe after bypass graft could not be resolved by a monoexponential analysis, but was closely approximated by two exponential delays which were termed "fast" and "slow" (Table I). In five patients (J. R., E. M., J. S., R. D., and N. G.) immediately after opening the bypass graft, a flow rate 5–6 times greater than the fast flow clearance was seen which lasted for 20–25 sec.

Preoperative arteriographic analyses. The mean values for arteriographic appearance time for each of the four arteriographic groups are summarized in Fig. 6 (upper left panel).

The mean appearance time for contrast agent to appear in vessel distal to an obstruction was significantly lower ($P < 0.025$) for group A vessels. Two appearance times were calculated for group C vessels since distal filling occurred by both antegrade and collateral sources. The mean antegrade arteriographic appearance time for group C vessels where collaterals were present was significantly longer than that for vessels in groups A and B where no collaterals were present. Mean appearance times for filling by collaterals were similar in groups C and D although collateral filling occurred earlier in group D vessels in which antegrade flow was not observed.

Intraoperative pressure-flow measurements. The mean values for preexisting MBF (graft clamped), preexisting distal vessel pressure (graft clamped), and pressure gradients across obstructions for each of the four arteriographic groups are summarized in Fig. 6. The preexisting blood flows with graft clamped (upper right panel) were near normal in group A vessels with less than 80% obstruction and no collaterals. In striking contrast, groups B, C, and D with greater than 80% occlusions had very low flows before opening the bypass graft. Similarly, the perfusion pressure in the distal coronary artery (lower left panel) for group A approached normal with the graft clamped, whereas in groups B, C, and D pressures were markedly reduced. Mean pressure gradients across obstructions (lower right panel) were very low for group A vessels with less than 80% occlusion, whereas for groups B, C, and D where obstructions were greater than 80%, the gradients were high. Groups C and D vessels with collateral blood supply did not have significantly higher preexisting flow (upper right panel) than group B vessels with a similar degree of obstruction and no collaterals ($P > 0.4$).

Fig. 7 demonstrates typical intraoperative data from a patient (L. B.) in group A with less than 80% obstruction in the proximal left anterior descending coronary artery. The intraoperative pressure gradient for this lesion (lower left panel) was 17 mm Hg. No change in precordial clearance of ^{133}Xe was seen after opening the bypass graft (upper right panel). The exponential plot of

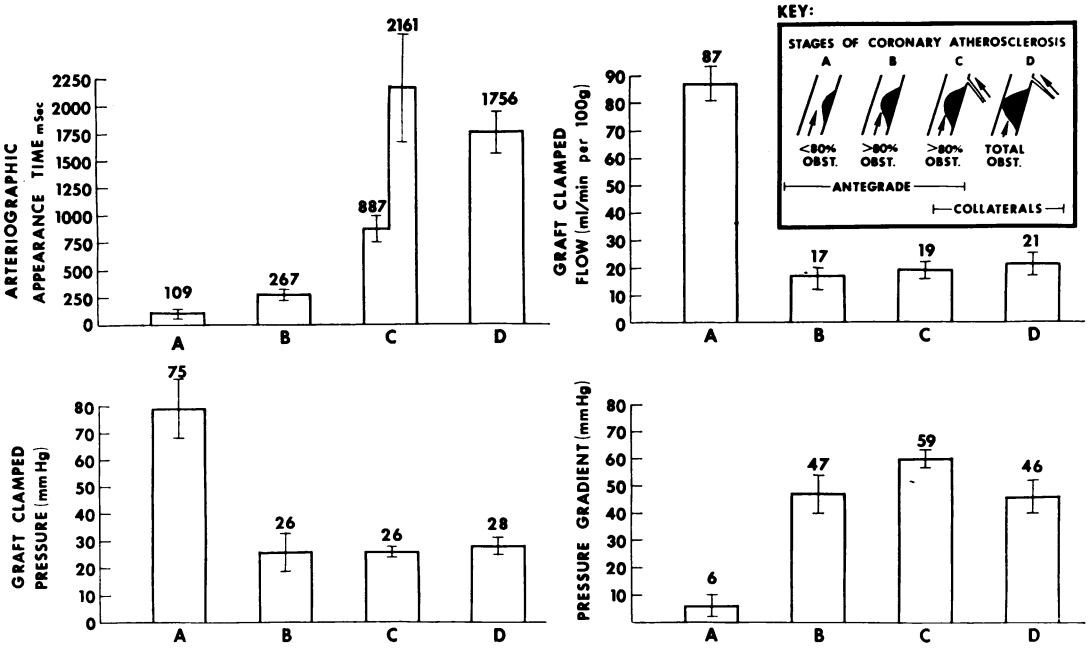

FIGURE 6 Summary of the mean arteriographic appearance times, graft clamped flows, graft clamped pressures, and pressure gradients across obstructions for each of the four stages of atherosclerosis. Values are mean ±SE. Value for both antegrade and collateral arteriographic appearance time are shown for group C.

the ^{133}Xe clearance curve (lower right panel) showed a rapid phase flow of 106 ml/min per 100 g and a slow phase of 13 ml/min per 100 g.

^{133}Xe clearance from epicardial fat. In a majority of patients (Table I), when MBF was augmented by a bypass graft, the clearance of ^{133}Xe could not be resolved by a monoexponential analysis, but was closely approximated by two exponential decays termed fast and slow phases. These findings suggested heterogeneity of either tissue or perfusion or possibly both, as an explanation for the slow phase of the ^{133}Xe clearance curve. The possibility exists that the known sequestrations of ^{133}Xe in fat might be the source of tissue heterogeneity and the so-called "slow" phase of clearance. This was studied in seven patients by injecting ^{133}Xe directly into epicardial fat. These clearance curves were compared with the slow component of the curves obtained after injection into the open bypass graft. In all seven patients (Table II), the $t_{\frac{1}{2}}$ for epicardial fat injection was significantly longer than the $t_{\frac{1}{2}}$ for the slow phase of the MBF curves.

The comparison of ^{133}Xe clearance curves for myocardium and epicardial fat in a patient (M. R.) are shown in Fig. 8. The myocardial ^{133}Xe clearance curve (left) was best approximated by two exponential delays. The $t_{\frac{1}{2}}$ for the slow phase was less than one-half that of epicardial fat (right).

DISCUSSION

The results of this study demonstrate the efficacy of coronary artery bypass surgery in restoring flow to previously ischemic myocardium. The majority of vessels with significant stenosis (groups B, C, and D) showed striking increases in MBF when the bypass grafts were opened. The values for ^{133}Xe MBF after bypass graft are consistent with previous intraoperative studies using electromagnetic flowmeters (12–14). The clearance technique measures flow per unit mass of myocardium and gives actual nutrient flow. This differs from electromag-

TABLE II

^{133}Xe Clearance ($t_{\frac{1}{2}}$) for Epicardial Fat and Slow Component of Myocardial Blood Flow in Seven Patients

Patient	Epicardial fat $t_{\frac{1}{2}}$	Slow component MBF $t_{\frac{1}{2}}$
	msec	*msec*
M. R.	481	218
D. S.	650	250
J. S.	635	378
W. Y.	550	155
M. C.	470	227
M. G.	467	349
V. Y.	395	180

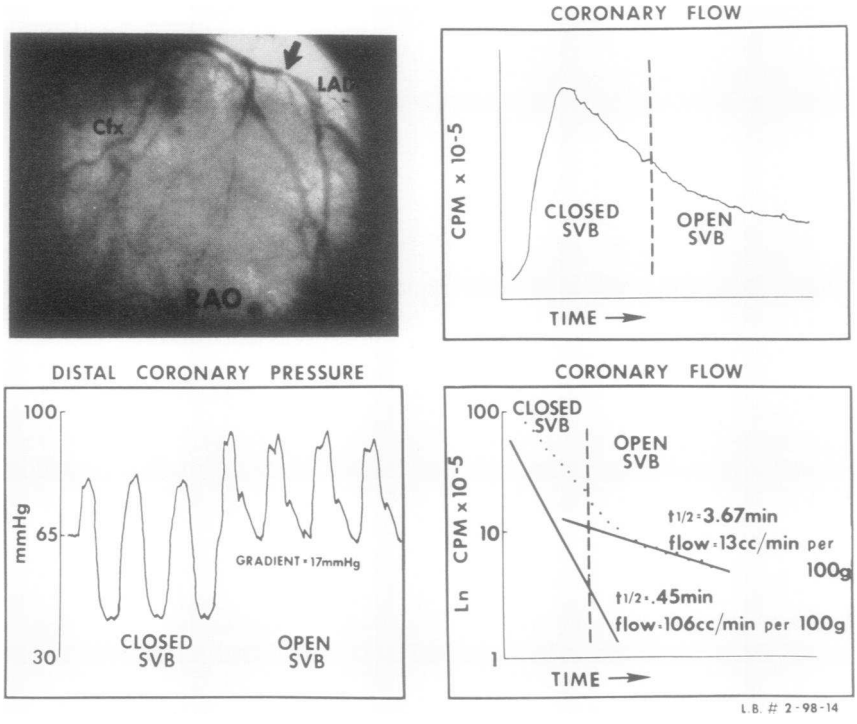

FIGURE 7 Results of arteriogram and intraoperative pressure and ^{133}Xe flow measurements for mild coronary artery obstruction.

netic flows which measure only total flow irrespective of its distribution. This report confirms the technical adequacy of bypass grafts in restoring nutrient flow to myocardium distal to a significant coronary arterial obstruction.

Of considerable interest are the results for vessels with small pressure gradients (group A), in which negligible increases in MBF were observed. In this group the preexisting pressure and flow were high, and the net contribution of bypass grafts to MBF in the rest state was minimal. Preoperative arteriography proved useful in identifying such vessels by virtue of the small degree of obstruction and the rapid appearance of contrast agent distal to an obstruction after selective coronary injection. Johnson, Flemma, and Leplay (15) and others (12–14, 16, 17) have observed a high incidence of graft occlusion in the presence of low graft flow rates. They attribute low flow either to technical errors with anastomosis, or to high resistance in distal vessels. The findings in the present study indicate that vessels with a minimal gradient across obstructions and a high preexisting flow and postobstructive pressure might form yet a third category subject to low graft flows and high incidence of early graft closure. Alternatively, under conditions augmenting the need for coronary flow, mild obstructions could assume functional significance, at which time flow via bypass graft would increase in response to a decrease in postobstructive pressure with distal vasodilation.

Recent experimental studies by Elliot, Bloor, Jones, Mitchell, and Gregg (1) in conscious dogs revealed that collateral flow measure by ^{133}Xe increased to control levels after 4 days of progressive coronary constriction. In similar studies in anesthetized dogs, Rees and Redding (2) demonstrated ^{133}Xe collateral flow to be 75% of control rates after acute ligation of the anterior descending coronary artery, with return toward control flow rates over a 10 day period. The results of the present study are not in accord with these experimental observations in the dog. Preexisting MBF was not significantly influenced by the presence of collaterals. The values for preexisting MBF in the presence of collateral circulation were less than one-third of normal rates of perfusion. Since all patients receiving bypass grafts were symptomatic, the vessels in the present study may have represented that portion of the total population of vessels receiving inadequate collateral flow. However, it is noteworthy that collateral flow was low in all vessels studied. Rees has alluded to variations in intercoronary anastomoses among species (18) and noted that they are more frequent in the dog than in man. The low values for collateral flow in the present study suggest that conclusions drawn from experimental data in animals, re-

garding collateral flow, may be of limited applicability in humans.

The low values for collateral flow documented by the present study may explain recent clinical observations in humans. Sheldon (3) has commented on the inability of collaterals to protect against infarction, and noted that collaterals alone are not likely to be responsible for complete remission of ischemic symptoms. Miller, Zelis, Mason, and Amsterdam (4) could find no significant enhancement of ventricular performance in association with arteriographically demonstrable collaterals in a matched group of 38 patients at cardic catheterization. Helfant, Kemp, and Gorlin (5) studied 111 patients with coronary disease and concluded the presence of collaterals did not protect against the development of asynergy or abnormal hemodynamics. In subsequent studies on the clinical effect of collaterals in 119 patients, Helfant, Vokonas, and Gorlin (6) concluded that collaterals had no demonstrable beneficial effect on the resting or exercise electrocardiogram. They found the patients with collaterals to have an incidence of acute myocardial infarction during a follow-up period which was nearly identical to a control group without collaterals.

The results of the arteriographic analyses from the present study suggest that coronary arterial obstructions become functionally significant as an 80% constriction of the lumen is approached. This observation is in accord with studies by Tuna and Amplatz (7), and Mason et al. (19) both of which found evidence of collateral formation with obstructions of 75% or greater. The precision by which per cent stenosis can be accurately determined from an arteriogram is variable. The results from the present study indicate that delayed appearance of contrast agent distal to an obstruction correlates well with the severity of the obstruction and provides a valuable adjunct in determining the significance of a given arteriographic obstruction. In the present study, the combination of 80% stenosis or greater, with prolonged arteriographic appearance times, was predictive of a high pressure gradient with marked reduction of postobstructive MBF even in the presence of collaterals.

In a majority of vessels, after MBF was augmented with a bypass graft, the clearance of ^{133}Xe could not be resolved by a monoexponential analysis but was closely approximated by two exponential decays. It is unlikely that the slow component was due either to recirculation or background count since greater than 95% of ^{133}Xe is removed on circulation through the lungs, the background counts in the room did not vary appreciably during the procedure and the proximity of probe to myocardium assured minimal counts from ^{133}Xe in the lungs and neighboring tissue. In general, the clearance curves were unaffected by either the duration of graft occlusion or variation in the sequence of isotope injection initially

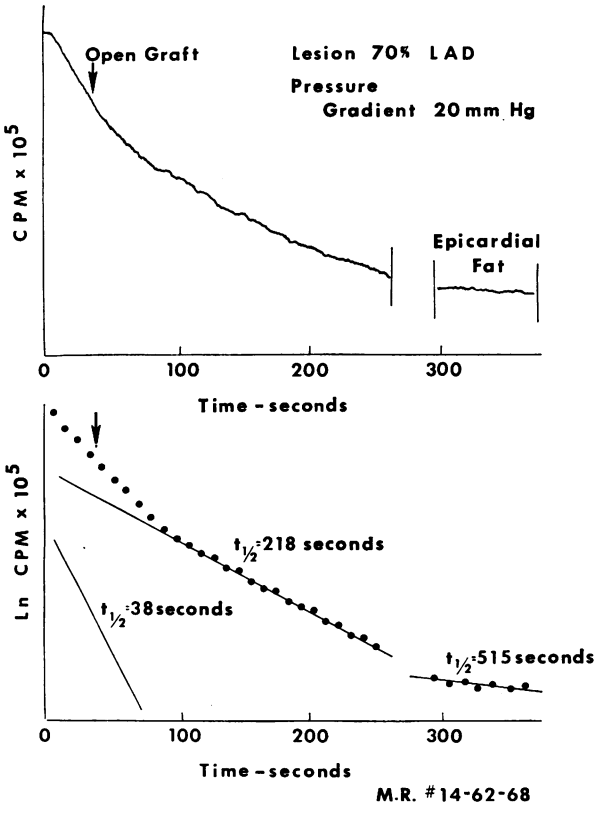

FIGURE 8 Comparative results for ^{133}Xe intraarterial myocardial blood flow and ^{133}Xe direct epicardial fat injection. LAD, left anterior descending artery.

with graft open or closed. However, as commented earlier, five patients did show a highly transient rapid clearance with initial opening of the graft and this may have been due to reactive hyperemia.

The persistence of a double exponential ^{133}Xe clearance pattern after augmentation of myocardial flow by bypass graft is theoretically consistent with a heterogeneity of myocardial tissue or perfusion pathways, or possibly both. Ross, Ueda, Lichtlen, and Rees (8) studied MBF using ^{133}Xe in normal dogs and found clearance from the normal myocardium to be best expressed by a monoexponential curve with good correlation with rotameter flows. Johansson, Linder, and Seeman (11) studied MBF using ^{85}krypton during acute coronary arterial occlusion in dogs. Monoexponential clearance curves were obtained before coronary arterial occlusion. After occlusion, clearance of ^{85}Kr was best resolved by two separate exponential components which they related to heterogeneity of flow. They observed a rapid phase related to the elimination of ^{85}Kr from normally perfused regions of the myocardium, and a slow phase due to decreased perfusion of the ischemic myocardium. In similar studies on anastomotic blood flow during experimental myocardial in-

farction in the dog using ^{133}Xe, Rees and Redding (2) also found that clearance curves were best resolved into fast and slow components which they related to uneven distribution of flow through the infarct.

Heterogeneity of myocardial flow has also been demonstrated in patients with coronary artery disease. In studying the effects of sublingual nitroglycerin on regional MBF, Horwitz, Gorlin, Taylor, and Kemp (20) found a double exponential decay pattern for diseased myocardium and suggested the slow phase was associated with collateral flow. Cannon, Dell, and Dwyer (21), using a multiple-crystal scintillation camera to study patients with coronary artery disease, found regional variations in ^{133}Xe clearance constants demonstrating heterogeneity of myocardial perfusion. They observed a significant reduction in clearance recorded by crystals overlying myocardium distal to arterial constrictions greater than 75%. Klocke et al. (22) demonstrated nonuniform myocardial clearance of hydrogen in patients with coronary artery disease which they related to heterogeneous flow.

Alternatively, the nonuniform myocardial clearance of ^{133}Xe may result from tissue heterogeneity. The partition coefficient for fat is 8–10 times that for myocardium (23). Bassingthwaighte, Strandell, and Donald (24) observed a persistent tailing of ^{133}Xe MBF curves in normal dogs which they attributed to changes in partition coefficient due to variations in the amount of adipose tissue from basal to apical regions of the heart. In the present study, clearance of ^{133}Xe from epicardial fat was significantly slower than the slow phase from myocardial clearance curves, indicating that fat alone did not account for the nonuniform myocardial clearance of ^{133}Xe.

The most plausible explanation for persistence of nonuniform ^{133}Xe clearance in the revascularized myocardium is a combined heterogeneity of altered perfusion pathways and varying myocardial partition coefficients. Both of these are the direct consequence of coronary artery disease. The revascularized myocardium probably includes a wide spectrum of pathologic changes with varying degrees of inflammation, lipid deposition, and fibrosis. The partition coefficient for each of these tissues is different and would result in altered clearance of ^{133}Xe. The differences in perfusion may be explained by persistent abnormalities in the distal large coronary arteries not corrected by revascularization and deviations in the microcirculatory pathways due to prior destruction of tissue with fibrosis.

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