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# Regional Myocardial Blood Flow Redistribution as a Cause of Postprandial Angina Pectoris

Ragavendra R. Baliga, MD; Stuart D. Rosen, MD; Paolo G. Camici, MD; Jaspal S. Kooner, MD, FRCP

**Background**—Postprandial angina pectoris has been recognized for more than two centuries and can be identified in up to 10% of patients with chronic ischemic heart disease. Redistribution of myocardial blood flow, from a region supplied by a severely stenotic coronary artery to those supplied by less diseased or normal vessels, is a potential mechanism of postprandial angina.

**Methods and Results**—To test this hypothesis, we have determined the effects of a standard liquid meal on whole heart and regional myocardial blood flow, measured by means of dynamic positron emission tomography (PET) with  $^{15}\text{O}$ -labeled water in 14 patients with a reproducible history of postprandial angina and 7 matched control subjects. The standard liquid meal precipitated angina pectoris in all patients. Baseline whole heart blood flow was similar and increased normally after the meal in patients ( $0.97 \pm 0.14$  to  $1.14 \pm 0.25 \text{ mL} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$ ,  $P < .04$ ) as in control subjects ( $0.92 \pm 0.12$  to  $1.02 \pm 0.13 \text{ mL} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$ ,  $P < .02$ ). In contrast, the coefficient of variation of blood flow increased significantly after the standard liquid meal in patients ( $34 \pm 9\%$ ,  $P < .05$  versus baseline) but not in control subjects ( $17 \pm 7\%$ ,  $P = \text{NS}$  versus baseline). In patients, analysis of regional myocardial blood flow demonstrated decreased myocardial blood flow in territories supplied by stenotic arteries ( $1.01 \pm 0.35$  to  $0.76 \pm 0.27 \text{ mL} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$ ,  $P < .03$ ), but there was an increase in blood flow in territories supplied by normal arteries ( $0.89 \pm 0.16$  to  $1.34 \pm 0.25 \text{ mL} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$ ,  $P < .001$ ) after the meal.

**Conclusions**—The standard liquid meal induced angina pectoris in patients with coronary artery disease. Although whole heart blood flow increased appropriately for the greater cardiac work, there was a redistribution of regional blood flow from territories supplied by severely stenosed coronary arteries to those supplied by less diseased or normal arteries. This redistribution may be the cause of myocardial ischemia in postprandial angina. (*Circulation*. 1998;97:1144-1149.)

**Key Words:** angina ■ food ■ coronary disease ■ blood flow

Postprandial angina pectoris has been recognized for more than two centuries and can be identified in up to 10% of patients with chronic ischemic heart disease.<sup>1</sup> It is even more common in patients with severe coronary artery disease and unstable angina.<sup>1,2</sup> The pathophysiological basis of postprandial angina is not fully understood.

Reduction in myocardial blood flow, caused by redistribution of blood from the coronary to the splanchnic vascular bed or to exercising muscles (in exertional postprandial angina), has been proposed as a possible mechanism in postprandial angina.<sup>1</sup> However, studies in animals<sup>3</sup> and in healthy human volunteers<sup>4</sup> have not provided support for this hypothesis. Others have suggested that an increase in cardiac work may have an important role in postprandial angina.<sup>2,5,6</sup> Indeed, the heart rate does increase after food both in normal subjects<sup>7</sup> and in patients with postprandial angina<sup>6,8</sup>; however, the magnitude of this rise is not sufficient to cause a significant increase in myocardial oxygen consumption.<sup>2,5,6</sup> Evidence from previous studies suggests that stimuli increasing sympathetic nervous activity, such as increased heart rate,

mental stress, and cold pressor, can reduce regional myocardial blood flow to below resting levels.<sup>9-11</sup> Similar changes may occur in severely diseased vessels during sympathetic activation after food. Redistribution of myocardial blood flow from regions supplied by a severely stenosed coronary artery to those supplied by less diseased, or normal vessels, might offer an explanation for postprandial angina. To test this hypothesis, we have determined the effects of a standard liquid meal on whole heart and regional myocardial blood flow by using positron emission tomography (PET) with  $^{15}\text{O}$ -labeled water in patients with a reproducible history of postprandial angina.

## Methods

### Study Population

We studied 14 consecutive patients, 12 men and 2 women  $62 \pm 6$  years old (mean  $\pm$  SD), with a clear and reproducible history of postprandial angina defined as typical chest pain in the resting state up to 1 hour after a standard liquid meal. All patients had angiographically proven coronary artery disease (at least one epicardial

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arterial stenosis of >70% luminal diameter and a dominant right coronary artery), and 8 patients had a previous history of myocardial infarction. All had stable symptoms. The treadmill exercise ECG test was positive for ischemia (>0.1 mV rectilinear or downsloping ST-segment depression 80 ms after the J point) in all patients. Seven normal healthy male subjects  $55 \pm 11$  years old ( $P = NS$  versus patients), selected from hospital staff, were studied as control subjects. None had cardiovascular symptoms or were receiving any medication. All had normal resting ECG, a normal exercise ECG at high workload, and normal thallium-201 myocardial perfusion scan at rest and during exercise.

### Study Protocol

Antianginal medication (except sublingual nitrates) was discontinued 14 days, and oral nitrates 24 hours, before the study day. All subjects abstained from caffeine-containing drinks for 24 hours before the PET study. The PET studies were performed after an overnight fast, between 8 and 9 AM, with subjects in the supine position. A standard liquid meal was administered over 10 minutes by a drinking straw with subjects in the supine position. The meal comprised 500 mL of fresh full cream milk (energy value, 64 kcal per 100 mL; total, 352 kcal, composed of 18.15 g protein, 25.85 g carbohydrate, and 19.25 g fat), plus 261.5 g of Complian (Heinz Ltd), a vitamin- and mineral-fortified drink mix, with dried skimmed milk and vegetable oil. The 261.5 of Complian consisted of 40.27 g protein, 159.78 g carbohydrate, and 38.70 g of fat. The total energy value of the 261.5 g of Complian was 1148, giving a total value of the liquid meal of 1500 kcal. In all patients and control subjects, simultaneous heart rate, blood pressure (Dinamap, Critikon Inc), and whole heart and regional myocardial blood flow measurements were made before and exactly 30 minutes after a standard liquid meal. The patients were monitored for symptoms and the time to onset of angina. A 12-lead ECG (Mac 6, Marquette Electronics) was recorded (1) under baseline conditions; (2) immediately after consuming the meal; (3) at the onset of angina; and (4) after the angina had resolved. The project was approved by the Research Ethics Committee, Hammersmith Hospital, and the UK Administration of Radioactive Substances Advisory Committee (ARAC). Written informed consent was obtained in each case. The study conformed to Declaration of Helsinki principles.

### Positron Emission Tomography

PET scans were performed at the Medical Research Council Cyclotron Unit, Hammersmith Hospital, with an ECAT 931 to 08/12 multislice positron scanner (CTI/Siemens). The scanner comprises eight rings of bismuth germanate detectors, allowing 15 cross-sectional images of the heart to be viewed simultaneously in a 10.5-cm axial field of view. Emission scans were reconstructed with a Hanning filter with cut-off at the Nyquist frequency. The transaxial resolution achieved was  $8.4 \pm 0.7$  mm, full width at half-maximum, for the emission data at the center of the field of view.

With the patient in the supine position, a 5-minute rectilinear transmission scan was recorded with a ring source of  $^{68}\text{Ge}$  initially to facilitate the positioning of the left ventricle within the window of view of the scanner. Subsequently a 20-minute transmission was performed to correct all emission scans for tissue attenuation. After the transmission scan, radioactive gases were delivered at a constant rate by a standard facemask used clinically for delivering oxygen (MC oxygen mask, Henlys Medical). A blood pool scan was performed by inhalation of  $^{15}\text{O}$ -labeled carbon monoxide ( $\text{C}^{15}\text{O}$ ), delivered at a rate of 500 mL/min, with 3 MBq/mL activity for 4 minutes. The inhaled  $\text{C}^{15}\text{O}$  rapidly forms [ $^{15}\text{O}$ ]carboxyhemoglobin. A single-frame, 6-minute scan was started 1 minute after the end of inhalation of the  $\text{C}^{15}\text{O}$ . After a 10-minute period (corresponding to approximately 5 half-life periods of  $^{15}\text{O}$ ) to allow for decay,  $^{15}\text{O}$ -labeled carbon dioxide ( $\text{C}^{15}\text{O}_2$ ) was administered for 3.5 minutes with 4 MBq/mL activity at a rate of 500 mL/min. The  $\text{C}^{15}\text{O}_2$  is immediately converted to  $\text{H}_2^{15}\text{O}$  by carbonic anhydrase in the lung.<sup>12</sup> A 25-frame scan was recorded commencing 30 seconds before  $\text{C}^{15}\text{O}_2$  delivery and continuing for a total of 7 minutes. A build-up scan over 3.5 minutes and a washout scan over 3 minutes are thus produced

(frame durations were  $1 \times 30$  seconds,  $6 \times 5$  seconds,  $6 \times 10$  seconds,  $6 \times 20$  seconds, and  $6 \times 30$  seconds).

### PET Data Analysis

The sinograms obtained were corrected for attenuation and reconstructed on a MicroVAX II computer (Digital Equipment Corporation), with dedicated array processors and standard reconstruction algorithms. Images were transferred to a SUN 3/60 workstation for further analysis with Analyze (Mayo Foundation)<sup>13</sup> and Pro-Matlab (The Mathworks Inc) software packages.

The reslicing of the images from the transaxial into the short-axis views was performed as follows. For the definition of the reslice parameters, the Heartool graphical user interface (CTI/Siemens) was used. The optimal transaxial slice was selected, generally that in which the left ventricular component of the image was largest. A guiding line was drawn on the latter image from the left ventricular apex, through the middle of the chamber, to the base of the left ventricle. The left ventricle was sliced parallel to this guiding line to produce oblique slices. The optimal left ventricular oblique slice was then selected (again, this was generally the oblique slice in which the left ventricular component of the image was largest). A guide line was drawn along the long axis, from the apex to the base of the left ventricle, on this optimal oblique slice. The program was used to define slices perpendicular to the long line of the oblique view. With the reslice parameters thus defined, the act of reslicing was carried out with an in-house reslicing program, which applies the reslice parameters defined with Heartool, to the images being resliced.

The blood volume image was produced from the  $\text{C}^{15}\text{O}$  data by dividing the raw image by the product of the average venous blood radioactivity and blood density (1.06 g/mL). Regions of interest were drawn within the left atrium on three consecutive image planes and projected onto the dynamic  $\text{H}_2^{15}\text{O}$  images to generate time-activity curves for these regions, the average being used as an arterial input function. An extravascular volume image (VEV) was constructed by subtraction of the blood volume image from the normalized transmission image. The normalization was achieved by first rescaling the transmission image such that the mean pixel count in a region of interest situated in the left ventricle was 1.06 (the density of blood). A conversion from milliliters to grams of tissue was then made by dividing by the density of tissue (1.04 g/mL). After this, the blood volume images were subtracted from the integrated time frames of the washout phase of the  $\text{H}_2^{15}\text{O}$  scans. The VEV and extravascular  $\text{H}_2^{15}\text{O}$  images were used for the delineation of four myocardial regions of interest corresponding to the territories of distribution of the major coronary arteries—septal, anterior, lateral, and inferoposterior—over five to eight short-axis planes of the left ventricle. The regions of interest were based on the outer section of  $4 \times 90$  degree quadrants applied on visual inspection by the investigators analyzing the PET data. (The investigators analyzing the PET data were blinded with respect to the subjects of the PET scans being patients or control subjects, as well as with respect to the patients' angiographic data.) In patients with stenosis of the left anterior descending artery, the anterior and septal regions were designated as the stenosis-related regions. In patients with stenosis of the right coronary artery, the inferoposterior region was designated as the stenosis-related region, and in those with stenosis of the left circumflex artery, the lateral region was designated as the stenosis-related region. Coronary stenoses were scored as 0% to 30%, 30% to 50%, 50% to 70%, 70% to 90%, and 90% to 100%. Lesions <50% were classified as nonstenotic and >90% as stenotic. The regions of interest were superimposed onto the kinetic time frames recorded during the  $\text{C}^{15}\text{O}_2$  inhalation and washout; this produced a plane-averaged time-activity curve for each region, which, together with the arterial input function, were fitted to a single tissue compartment tracer kinetic model to give values for regional MBF ( $\text{mL} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$ ) as previously reported.<sup>14</sup> In addition, whole heart MBF was determined by defining additional regions of interest, each drawn to encompass the whole of the left ventricle within each image plane. These whole heart regions were superimposed onto the kinetic time frames as described above for the subregions to provide a single whole left ventricle time-activity curve before the calculation of

TABLE 1. Hemodynamic Responses to the Standard Liquid Meal in Patients With Postprandial Angina and in Control Subjects

	Age, y	Heart Rate, bpm		Systolic Blood Pressure, mm Hg		Diastolic Blood Pressure, mm Hg		Heart Rate × Blood Pressure		
		Basal	Meal	Basal	Meal	Basal	Meal	Basal	Meal	Treadmill
Patients										
1	68	57	78	201	250	85	136	7581	14 586	12 400
2	49	57	63	109	107	77	69	5187	5040	7150
3	63	50	51	186	175	82	76	6100	5559	8360
4	54	60	79	175	185	87	91	6960	9401	8840
5	65	52	60	106	105	69	65	4264	5100	4150
6	69	70	78	167	157	87	73	8960	8424	9760
7	68	72	82	126	121	66	73	6552	7380	9280
8	65	52	61	135	154	66	78	5148	6527	7410
9	58	60	58	120	113	77	68	5640	4814	8130
10	55	42	53	128	123	67	66	3612	4399	5680
11	68	68	61	149	151	81	84	7072	6466	7270
12	59	65	60	136	138	72	74	6045	5640	4130
13	67	53	56	173	184	84	75	5671	6104	8320
14	61	71	87	130	127	82	84	7029	8787	9360
Control Subjects										
1	61	60	66	103	105	68	68	6798	7560	
2	51	61	66	128	121	71	70	8064	7744	
3	58	71	78	122	136	77	74	8296	10 472	
4	69	65	69	131	122	75	67	8777	8906	
5	62	70	76	135	144	74	70	9045	10 224	
6	49	67	66	101	108	63	65	5959	7344	
7	35	75	85	121	126	77	66	7744	10 458	

MBF. Thus whole heart and regional values of MBF were obtained. In addition, the coefficient of variation of flow (COV) was also derived for MBF at rest and after the liquid meal as an index of homogeneity of low distribution. The COV was calculated per subject as the standard deviation/mean of the whole heart MBF values, expressed as a percentage.

### Plasma Catecholamines

Blood samples for catecholamines were collected by an indwelling venous cannula in the antecubital fossa, in lithium-heparin tubes containing ethylene glycol-tetra acetic acid and reduced glutathione. Samples were taken in the basal fasting state and 30 minutes after the meal. The tubes were placed immediately on ice. Plasma was separated by refrigerated centrifugation and stored at  $-70^{\circ}\text{C}$ . Plasma norepinephrine and epinephrine were determined by high-power liquid chromatography.<sup>15</sup> The assay is sensitive to 20 pg/mL. The within-run coefficient of variation is  $<7.5\%$ . Interassay variability was 10% to 15%, and all samples were assayed together.

### Statistical Analysis

All values are expressed as mean  $\pm$  SD. The two-tailed unpaired Student's *t* test was used to compare the data on age, heart rate, blood pressure, and rate-pressure product between the patient and control groups. Differences in basal and postprandial whole heart and regional myocardial blood flow responses were examined with one-way ANOVA and Scheffé's test. Comparison within subjects between resting and postprandial heart rates, blood pressures, and rate-pressure products and myocardial blood flow were made with Student's paired *t* test. A value of  $P < .05$  was considered statistically significant.

## Results

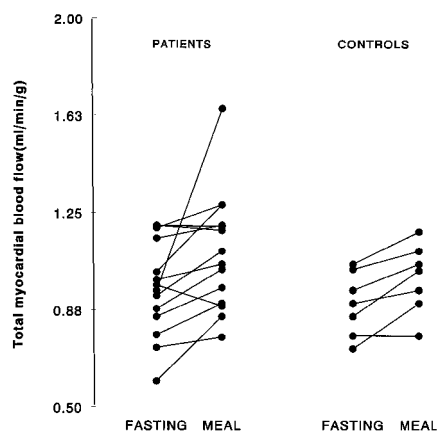
### Clinical Observations

Twelve of the 14 patients developed characteristic anginal symptoms within 22 to 30 minutes of the meal. Seven patients additionally developed ischemic ECG changes. Control subjects did not have symptoms or ECG changes.

Basal heart rate and blood pressure were similar in patients and control subjects. Thirty minutes after the standard liquid meal, heart rate increased but blood pressure was unchanged in patients and control subjects. The heart rate  $\times$  systolic blood pressure product (RPP), an indirect index of myocardial oxygen consumption, was not significantly different at the onset of angina or during chest discomfort 30 minutes after the meal compared with baseline measurements in patients. The heart rate  $\times$  systolic blood pressure product was increased 30 minutes after the meal compared with basal levels in control subjects (Table 1).

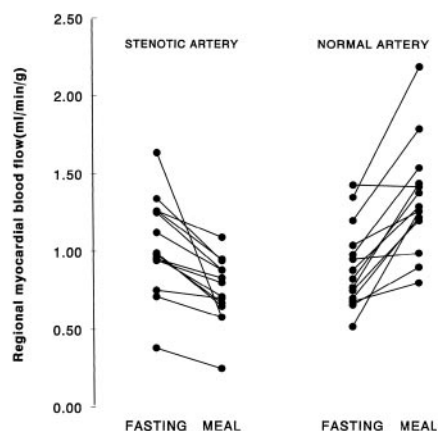
### Positron Emission Tomography

Twelve of the 14 patients had chest discomfort during whole heart and regional blood flow measurements 30 minutes after the meal. Baseline whole heart blood flow was not significantly different and increased to a similar extent after the standard liquid meal in patients ( $0.97 \pm 0.14$  to  $1.14 \pm 0.25$  mL  $\cdot$  min $^{-1} \cdot$  g $^{-1}$ ,  $P < .04$ ) and in control subjects ( $0.92 \pm 0.12$



**Figure 1.** Total myocardial blood flow in the basal state and after the standard liquid meal in patients with postprandial angina ( $n=14$ ) and in control subjects ( $n=7$ ).

to  $1.02 \pm 0.13 \text{ mL} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$ ,  $P < .02$ ). After correcting for the prevailing heart rate–blood pressure product, whole heart blood flow did not show an increase after the standard liquid meal in patients ( $1.64 \pm 0.44$  to  $1.77 \pm 0.76$ ) or control subjects ( $1.12 \pm 0.24$  to  $1.17 \pm 0.30$ ). The baseline coefficient of variation of blood flow (COV) was similar in patients and control subjects ( $19 \pm 10\%$  versus  $13 \pm 5\%$ ,  $P = \text{NS}$ ). However, COV increased significantly after the meal in patients ( $34 \pm 9\%$ ,  $P < .05$ , versus baseline) but not in control subjects ( $17 \pm 7\%$ ,  $P = \text{NS}$  versus baseline, Fig 1). In the patient group, comparison of myocardial blood flow was made between territories supplied by the stenotic arteries and those supplied by nonstenotic coronary arteries. Baseline myocardial blood flow was not significantly different in regions subtended by stenotic and the nonstenotic coronary arteries. After the meal, myocardial blood flow fell in regions subtended by stenotic arteries ( $1.01 \pm 0.35$  to  $0.76 \pm 0.27 \text{ mL} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$ ,  $P < .03$ ) but increased in regions subtended by nonstenotic arteries ( $0.89 \pm 0.16$  to  $1.34 \pm 0.25 \text{ mL} \cdot \text{min}^{-1} \cdot \text{g}^{-1}$ ,  $P < .001$ , Fig 2). Calculated coronary vascular resistance index increased in stenotic ( $111 \pm 62$  to  $155 \pm 89$  arbitrary units,  $P < .001$ ) but decreased in nonstenotic ( $119 \pm 38$  to  $80 \pm 29$  arbitrary units,  $P < .001$ ) arteries after the meal.



**Figure 2.** Regional myocardial blood flow in territories supplied by stenotic and normal arteries, in the fasting state, and after the standard liquid meal in patients with postprandial angina.

### Plasma Catecholamines

Plasma norepinephrine increased after the meal in patients ( $3.9 \pm 0.3$  to  $5.1 \pm 0.4 \text{ pmol/mL}$ ,  $P < .002$ ) and control subjects ( $3.3 \pm 0.3$  to  $4.8 \pm 0.3 \text{ pmol/mL}$ ,  $P < .002$ ). Plasma epinephrine did not change after the meal in patients ( $0.67 \pm 0.1$  to  $0.79 \pm 0.2 \text{ pmol/mL}$ ) or in control subjects ( $0.63 \pm 0.2$  to  $0.78 \pm 0.2 \text{ pmol/mL}$ ).

### Discussion

The principal findings of this study are that postprandial angina is associated with: (a) a normal increase in whole heart myocardial blood flow and (b) significant redistribution of regional myocardial blood flow, from territories supplied by severely stenosed arteries to those supplied by less diseased or normal coronary arteries.

Postprandial angina has been attributed to reduced myocardial blood flow because of redistribution of flow from the coronary arteries to the splanchnic vascular bed<sup>8</sup> or to exercising muscles (in exertional postprandial angina).<sup>1</sup> However, our observations, based on direct measurement of blood flow, using PET, indicate that whole heart blood flow increases normally after the standard liquid meal in patients with postprandial angina. An increase in cardiac work has also been suggested as a possible mechanism in postprandial angina.<sup>2,5,6</sup> In this study the standard liquid meal induced a significant increase in heart rate in postprandial angina patients<sup>6,8</sup> and in control subjects.<sup>16,17</sup> However, the magnitude of the rise in heart rate was not sufficient to produce a significant change in the rate–pressure product, a quantity known to increase linearly with myocardial oxygen consumption in normal subjects.<sup>18</sup> It is well known that blood pressure is an important determinant of myocardial blood flow, and it is entirely consistent that whole heart blood flow after the standard liquid meal is not significant if corrected for the prevailing myocardial workload. However, it is not within the scope of the current study to examine the relation between the relative regional myocardial contributions to total cardiac work and regional myocardial blood flow data. A possible role for regional myocardial work, in influencing regional myocardial blood flow patterns, cannot be excluded from results of this study.

There was an increase in plasma norepinephrine after the meal in patients and control subjects (Table 2). This is likely to have resulted from sympathetic activation and is absent after the meal in patients with primary autonomic failure.<sup>19</sup> In normal subjects, the net effect of stimuli increasing sympathetic nervous activity is coronary vasodilatation with an increase in myocardial blood flow.<sup>9–11</sup> In patients with coronary artery disease, the coronary vasodilator reserve is exhausted in territories supplied by arteries with stenoses  $>80\%$  of the luminal diameter.<sup>20</sup> In such severely diseased vessels, stimuli increasing sympathetic nervous activity, such as increased heart rate, mental stress, and cold-pressor, can reduce regional myocardial blood flow to below resting levels,<sup>9–11</sup> and the sympathetic activation due to food ingestion may have the same effect. Consistent with this, we found that in our patients, the standard liquid meal increased calculated coronary vascular resistance in regions supplied by stenotic arteries but reduced vascular resistance in regions

**TABLE 2. Whole Heart and Regional Myocardial Blood Flow Responses (in mL · min<sup>-1</sup> · g<sup>-1</sup>) to the Standard Liquid Meal in Patients With Postprandial Angina and in Control Subjects**

	Septal		Anterior		Lateral		Inferior		Whole Heart	
	Basal	Meal	Basal	Meal	Basal	Meal	Basal	Meal	Basal	Meal
Patients										
1	0.82	1.38	0.93	1.29	1.06	1.08	0.96	0.71	0.93	1.11
2	0.96	1.44	1.35	2.19	1.25	0.88	0.78	0.84	1.02	1.28
3	0.68	0.80	0.92	1.03	0.89	0.82	0.38	0.25	0.73	0.77
4	0.75	1.21	0.79	0.85	1.26	0.95	1.07	1.19	0.89	1.03
5	0.75	0.70	0.66	0.90	0.81	1.17	0.62	0.79	0.69	0.85
6	1.13	1.06	1.04	1.26	0.84	0.90	0.71	0.58	1.20	1.20
7	1.04	0.91	1.65	0.58	1.24	1.50	0.98	1.55	1.20	1.18
8	1.04	0.99	1.21	1.78	1.18	1.69	1.12	0.88	1.15	1.21
9	0.82	1.21	0.88	1.30	0.89	0.78	0.99	0.65	0.85	0.96
10	0.77	1.44	1.11	2.31	1.34	0.94	0.67	1.19	0.95	1.65
11	1.02	1.07	1.13	1.49	1.26	1.09	0.70	1.22	0.99	1.05
12	1.11	1.18	1.43	1.42	1.21	1.62	0.98	0.67	1.19	1.28
13	1.04	0.99	0.95	0.99	0.93	0.80	0.94	0.80	0.97	0.89
14	0.77	0.73	0.95	0.83	0.81	1.01	0.52	1.26	0.78	0.90
Control Subjects										
1	0.82	1.03	1.11	1.22	1.09	0.96	0.88	0.74	0.95	1.10
2	1.31	1.5	1.06	1.08	0.97	1.1	1.07	1.21	1.10	1.20
3	0.72	0.8	0.8	0.94	1.00	0.8	0.69	0.68	0.78	0.78
4	0.92	1.05	0.88	0.97	0.86	1.09	0.86	1.08	0.89	1.04
5	0.96	1.02	1.04	1.18	1.04	1.01	1.33	1.4	1.10	1.13
6	0.88	1.01	1.12	1.16	0.86	0.98	0.77	0.71	0.90	0.96
7	0.79	0.98	0.96	1.09	1.00	1.14	0.79	0.8	0.73	0.91

supplied by nonstenotic vessels. It may be hypothesized that in patients with severe coronary artery disease, adrenergically mediated coronary vasoconstriction cannot be overcome either by vasodilatation caused by the local action of the

products of metabolism or by local endothelium-derived relaxing factor nitric oxide<sup>10,11</sup>; release of the latter is known to be impaired in atherosclerotic segments. Vasodilatation of the coronary microcirculation in territories supplied by nor-

**TABLE 3. Coronary Anatomy, Symptoms, and ECG Changes After the Standard Liquid Meal in Patients With Postprandial Angina**

Patient	LAD	D1	LCA	OM1	RCA	ECG	Symptoms
						ST/T-Wave Change	Angina/Dyspnea
1	30–50	0–30	50–70	50–70	90	None	Yes
2	0–30	0–30	70–90	70–90	100	Inferior/lateral	Yes
3	30–50	0–30	30–50	100	90	None	Yes
4	30–50	50–70	90	90	100	Inferior/lateral	Yes
5	90	100	0–30	30–50	30–50	None	Yes
6	0–30	0–30	30–50	50–70	90	Inferior	Yes
7	100	90	50–70	100	0–30	Anterior/lateral	Yes
8	30–50	50–70	30–50	30–50	90	None	Yes
9	0–30	0–30	100	100	90	None	Yes
10	30–50	0–30	90	100	30–50	None	No
11	100	100	90	50–70	0–30	Anterior/lateral	No
12	100	100	30–50	100	90	None	Yes
13	70–90	100	100	100	90	Inferior/lateral	Yes
14	90	100	100	100	30–50	Anterior	Yes

LAD indicates left anterior descending coronary artery; D1, first diagonal branch of the LAD; LCA, left circumflex artery; OM1, first obtuse marginal branch of the LCA; and RCA, right coronary artery.

mal or less severely diseased arteries may consequently lead to diversion of blood from those territories supplied by more severely diseased arteries (Table 3).

Food ingestion is associated with the release of a variety of gastrointestinal hormones<sup>19,21</sup> as well as norepinephrine. The relative importance of these neurohormonal consequences in redistribution of myocardial blood flow in postprandial angina is not known. Direct noninvasive measurements of regional myocardial blood flow with PET after adrenoceptor antagonists or octreotide may allow the role of catecholamines and vasoactive gastrointestinal hormones to be investigated more fully. An investigation of the effect of meals of different food composition would also be of importance because previous studies indicate that postprandial angina results predominantly from the carbohydrate rather than fat or protein component.<sup>22</sup>

In conclusion, direct noninvasive measurements of myocardial blood flow after a standard liquid meal demonstrate that whole heart blood flow increases to the same extent in postprandial angina patients as in control subjects. In patients with postprandial angina, myocardial ischemia presumably results from redistribution of blood from regions supplied by stenotic coronary arteries to those subtended by nonstenosed coronary arteries. On the basis of these observations, postprandial angina might logically be prevented by drugs that selectively reduce adrenergically mediated coronary vasoconstriction in severely diseased coronary segments and those that oppose metabolic vasodilatation in territories supplied by less diseased or normal arteries.

## References

- Berlinerblau R, Shani J. Postprandial angina pectoris: clinical and angiographic correlations. *J Am Coll Cardiol*. 1994;23:627-629.
- Goldstein RE, Redwood DR, Rosing DR, Beiser GD, Epstein SE. Alterations in the circulatory response to exercise following a meal and their relationship to postprandial angina pectoris. *Circulation*. 1971;44:90-100.
- Vatner SF, Franklin DL, Van Citters RL. Changes in regional blood flow after eating. *Fed Proc*. 1969;28:586.
- Regan TJ, Binak K, Gordon S, DeFazio V, Hellems HK. Myocardial blood flow and oxygen consumption during postprandial lipemia and heparin-induced lipolysis. *Circulation*. 1961;23:55-63.
- Figueras J, Singh BN, Ganz W, Swan HJ. Haemodynamic and electrocardiographic accompaniments of resting postprandial angina. *Br Heart J*. 1979;42:402-409.
- Cowley AJ, Fullwood LJ, Stainer K, Harrison E, Muller AF, Hampton JR. Postprandial worsening of angina: all due to changes in cardiac output?. *Br Heart J*. 1991;66:147-150.
- Yi JJ, Fullwood L, Stainer K, Cowley AJ, Hampton JR. Effects of food on the central and peripheral haemodynamic response to upright exercise in normal volunteers. *Br Heart J*. 1990;63:22-25.
- Kelbaek H, Gjørup T, Christensen NJ, Munck O, Godtfredsen J. Central hemodynamic changes after ingestion of a meal in patients with coronary artery disease. *Arch Intern Med*. 1989;149:363-365.
- Nabel EG, Gordon JB, Alexander RW, Selwyn AP. Dilation of normal and constriction of atherosclerotic coronary arteries caused by the cold pressor test. *Circulation*. 1988;77:43-52.
- Nabel EG, Selwyn AP, Ganz P. Paradoxical narrowing of atherosclerotic coronary arteries induced by increases in heart rate. *Circulation*. 1990;81:850-859.
- Yeung AC, Vekshstein VI, Krantz DS, Vita JA, Ryan TJJ, Ganz P, Selwyn AP. The effect of atherosclerosis on the vasomotor response of coronary arteries to mental stress. *N Engl J Med*. 1991;325:1551-1556.
- West JB, Dollery CT. Uptake of oxygen-15-labelled CO<sub>2</sub> compared with carbon-11-labelled CO<sub>2</sub> in the lung. *J Appl Physiol*. 1962;17:9-13.
- Rob RA, Hanson DP. A software system for interactive and quantitative visualisation of multidimensional biomedical images. *Australas Phys Eng Sci Med*. 1991;14:9-30.
- Rosen SD, Uren NG, Kaski JC, Tousoulis D, Davies GJ, Camici PG. Coronary vasodilator reserve, pain perception, and sex in patients with syndrome X. *Circulation*. 1994;90:50-60.
- Bouloux P, Perrett D, Besser GM. Methodological considerations in the determination of plasma catecholamines by high performance liquid chromatography with electrochemical detection. *Ann Clin Biochem*. 1985;22:194-203.
- Kelbaek H, Munck O, Christensen NJ, Godtfredsen J. Central haemodynamic changes after a meal. *Br Heart J*. 1989;61:506-509.
- Lipsitz LA, Ryan SM, Parker JA, Freeman R, Wei JY, Goldberger AL. Hemodynamic and autonomic nervous system responses to mixed meal ingestion in healthy young and old subjects and dysautonomic patients with postprandial hypotension. *Circulation*. 1993;87:391-400.
- Camici P, Marraccini P, Marzilli M, Lorenzoni R, Buzzigoli G, Puntoni R, Boni C, Bellina CR, Klassen GA, L'Abbate A. Coronary hemodynamics and myocardial metabolism during and after pacing stress in normal humans. *Am J Physiol*. 1989;257:E309-E317.
- Mathias CJ, da Costa DF, Fosbraey P, Bannister R, Wood SM, Bloom SR, Christensen NJ. Cardiovascular, biochemical and hormonal changes during food-induced hypotension in chronic autonomic failure. *J Neurol Sci*. 1989;94:255-269.
- Hermansen F, Bloomfield PM, Ashburner J, Camici PG, Lammertsma AA. Linear dimension reduction of sequences of medical images, II: direct sum decomposition. *Phys Med Biol*. 1995;40:1921-1941.
- Kooner JS, Peart WS, Mathias CJ. The peptide release inhibitor, Octreotide (SMS201-995), prevents the haemodynamic changes following food ingestion in normal human subjects. *Q J Exp Physiol*. 1989;74:569-572.
- Baliga RR, Burden L, Sidhu MK, Rampling MW, Kooner JS. Postprandial angina results from the carbohydrate but not fat or protein component of the meal. *Am J Cardiol*. 1997;79:1397-1400.