Absence of Postprandial Surge in Coronary Blood Flow Distal to Significant Stenosis: A Possible Mechanism of Postprandial Angina

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OBJECTIVES
This study was designed to investigate a possible mechanism of postprandial angina. Postprandial angina has been recognized for more than two centuries; however, its mechanism is still controversial. The most widely accepted mechanism involves increased myocardial oxygen demand after food intake. Recently, the redistribution in coronary blood flow (CBF) has been suggested as a possible mechanism.

METHODS
Twenty young, healthy volunteer controls and 20 patients with significant stenosis in the left anterior descending (LAD) or left main coronary artery were enrolled in the study. Coronary blood flow was evaluated in the distal LAD by using transthoracic Doppler echocardiography before and 15, 30, 45, and 60 min after food intake. In the CBF curve, the time velocity integral of diastolic flow (Dvti) and the product of Dvti and heart rate (HR) were measured.

RESULTS
In the healthy volunteer controls, Dvti and Dvti × HR increased after food intake with a peak value at 15 min, which indicates the presence of postprandial surge in the CBF. Fasting values and peak values at 15 min were significantly different (Dvti: 15.1 ± 4.9 cm/s vs. 18.9 ± 5.9 cm/s, p = 0.04, Dvti × HR: 862.2 ± 261.5 cm/min vs. 1,174.2 ± 307.5, p = 0.002). In contrast with the controls, despite postprandial increase in double product (HR × blood pressure), Dvti and Dvti × HR in the patient group decreased after food intake, with a nadir value at 45 min. Fasting values and nadir values at 45 min were significantly different (Dvti: 24.0 ± 19.6 cm/s vs. 19.3 ± 17.1 cm/s, p < 0.001, Dvti × HR: 1,449.6 ± 1,044.0 cm/min vs. 1,273.4 ± 1,000.9 cm/min, p = 0.002). In six patients, the CBF pattern resumed the normal pattern of postprandial surge in the CBF after successful coronary intervention.

CONCLUSIONS
Results of our study suggest that "steal phenomenon" may play a role in the mechanism of postprandial angina. (J Am Coll Cardiol 2002;40:1976–83) © 2002 by the American College of Cardiology Foundation

The phenomenon of postprandial angina has been well recognized since it was first described by Herbeden in 1772 (1). However, its mechanism has not been clearly elucidated, though it has been postulated that increased myocardial oxygen demand after food intake precipitates angina (2–6).

In contrast with previous studies that have suggested increased myocardial oxygen demand as a mechanism of postprandial angina, a recent study (5) using positron emission tomography showed that myocardial blood flow decreases in the stenotic coronary artery territory during the postprandial period, suggesting a redistribution of myocardial blood flow as a possible cause of postprandial angina.

High-frequency pulse-wave Doppler echocardiography allows coronary blood flow (CBF) in the left anterior descending coronary artery (LAD) to be assessed non-invasively. Application of this modality in pathologic conditions is limited, as only the CBF in the LAD can be evaluated. However, given the modality's non-invasiveness, it is suitable for evaluating coronary physiology. In this study, we compared changes in CBF in the controls with changes in CBF in patients having significant stenosis in the LAD or in the left main coronary artery. In addition, we evaluated changes in the CBF pattern after significant stenosis had been relieved. The effect of sham feeding was evaluated to exclude any effects of simple gastric distension.

METHODS

Study subjects. Twenty patients with functionally significant stenosis of the LAD or the left main coronary artery were enrolled in the study. Functionally significant stenosis was defined as >75% stenosis by coronary angiogram and a reversible defect on sestamibi single photon emission computed tomography in the LAD territory during dipyridamole stress. Patients with resting angina, myocardial infarction, and previous percutaneous coronary intervention were excluded. Twenty healthy volunteers were enrolled as controls. Informed consent was obtained from all the volunteers and patients.
Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>BP</td>
<td>blood pressure</td>
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<tr>
<td>CBF</td>
<td>coronary blood flow</td>
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<tr>
<td>Drv 1</td>
<td>time velocity integral of the diastolic coronary flow</td>
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<tr>
<td>HR</td>
<td>heart rate</td>
</tr>
<tr>
<td>LAD</td>
<td>left anterior descending artery</td>
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<tr>
<td>SPECT</td>
<td>single photon emission computed tomography</td>
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Echocardiographic examination. Transthoracic echocardiographic examinations were performed after fasting for at least 6 h, and all medications were discontinued for at least 12 h before examination. Before coronary flow was evaluated, left ventricular dimensions, ejection fractions, wall thicknesses, left atrial dimension, and mitral inflow Doppler parameters were obtained. Coronary blood flow was evaluated by using a 7 MHz transducer (Sequioa, Acuson, Mountain View, California) at the distal LAD during end-expiratory apnea before and 15, 30, 45, and 60 min after food intake, together with blood pressure (BP) and heart rate (HR). The time-velocity integral of the diastolic flow (Drv1) was measured in the coronary flow velocity curve. The average value of three consecutive beats was used in the analysis. The standard meal was composed of 68 g of fat, 159 g of carbohydrate, and 37 g of protein, with a total calorie count of 1,382 Cal.

In six patients with successful percutaneous coronary intervention (two patients with balloon angioplasty and four with stenting), these measurements were repeated after the intervention. To evaluate the effect of simple gastric distension on the CBF, the CBF was assessed after the sham meal in five of the controls. Pure water (800 cm$^3$) was used as a sham meal.

Statistical analysis. Continuous variables are reported as mean ± SD, and categorical variables as numbers and percentages. Differences in categorical variables were compared using the Fisher exact test and chi-squared test. Differences in continuous variables were compared by the Mann-Whitney U test. The Wilcoxon signed-rank test was used in the analysis of the changes in continuous variables in a group. Statistical analysis was performed using SPSS 10.0 software (SPSS Inc., Chicago, Illinois), and a p value of <0.05 was considered statistically significant.

RESULTS

Clinical characteristics and echocardiographic parameters. All volunteer controls were men, and compared with the controls, the patients were older and had a higher prevalence of hypertension, diabetes, and history of smoking (Table 1). In the patient group, there were five patients with one-vessel disease, eight patients with two-vessel disease, six patients with triple-vessel disease, and one patient with left main disease. The controls showed lower ejection fractions and a lower prevalence of having abnormal relaxation (Table 2).

Postprandial changes in BP and HR. Controls and patients both showed similar trends in terms of changes in BP and HR after food intake. An increase in systolic BP and a decrease in diastolic BP—therefore, increase in pulse pressure—and increase in HR were observed after food intake (Fig. 1).

Changes in coronary blood flow after food intake. In the controls, Drv1 and Drv1 × HR increased after food intake, with the peak value 15 min after food intake. Fasting values and peak values at 15 min were significantly different (Drv1: 15.1 ± 4.9 cm/s vs. 18.9 ± 5.9 cm/s, p = 0.04, Drv1 × HR: 862.2 ± 261.5 cm/min vs. 1,174.2 ± 307.5, p = 0.002). In patients, Drv1 and Drv1 × HR decreased after food intake with a nadir value 45 min after food intake. Fasting values and nadir values at 45 min were significantly different (Drv1: 24.0 ± 19.6 cm/s vs. 19.3 ± 17.1 cm/s, p < 0.001, Drv1 ×

### Table 1. Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Volunteers (n = 20)</th>
<th>Patients (n = 20)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>24.5 ± 3.1</td>
<td>59.8 ± 8.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Men (%)</td>
<td>20 (100%)</td>
<td>16 (86%)</td>
<td>0.035</td>
</tr>
<tr>
<td>HR (/min)</td>
<td>58 ± 9</td>
<td>64 ± 13</td>
<td>0.13</td>
</tr>
<tr>
<td>HTN</td>
<td>0</td>
<td>7 (35%)</td>
<td>0.008</td>
</tr>
<tr>
<td>DM</td>
<td>0</td>
<td>6 (30%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Smoking</td>
<td>6 (30%)</td>
<td>12 (60%)</td>
<td>0.06</td>
</tr>
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*Continuous variables by the Mann-Whitney U test and categorical variables by the Fisher's exact test and chi-squared test.

DM = diabetes mellitus; HR = heart rate; HTN = hypertension.

### Table 2. Echocardiographic Parameters in Healthy Volunteers and in Patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Volunteers (n = 20)</th>
<th>Patients (n = 20)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDD (mm)</td>
<td>49.5 ± 3.6</td>
<td>52 ± 6.6</td>
<td>0.647</td>
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<tr>
<td>EF (%)</td>
<td>55.9 ± 6.5</td>
<td>62.6 ± 10.5</td>
<td>0.006</td>
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<tr>
<td>IVS/LVPW (mm)</td>
<td>9.1 ± 1.1/8.7 ± 0.7</td>
<td>12.1 ± 1.5/11.2 ±1.8</td>
<td>&lt;0.001/&lt;0.001</td>
</tr>
<tr>
<td>LA (mm)</td>
<td>33.1 ± 2.5</td>
<td>39.2 ± 3.7</td>
<td>0.001</td>
</tr>
<tr>
<td>E/A (m/s)</td>
<td>0.83 ± 0.16/0.44 ± 0.13</td>
<td>0.68 ± 0.14/0.83 ± 0.20</td>
<td>0.01/&lt;0.001</td>
</tr>
<tr>
<td>DT (ms)</td>
<td>153 ± 32</td>
<td>227 ± 52</td>
<td>&lt;0.001</td>
</tr>
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</table>

*By the Mann-Whitney U test.

A = peak velocity of late mitral inflow; DT = deceleration time of early mitral inflow; E = peak velocity of early mitral inflow; EF = ejection fraction; IVS = interventricular septal thickness; LA = left atrial dimension; LVEDD = left ventricular end-diastolic dimension; LVEDD = left ventricular end-systolic dimension; LVPW = left ventricular posterior wall thickness.
Figure 1. Changes in systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and double product after food intake. Controls and patients both showed similar patterns of change. Solid line = patients; dotted line = controls.

Figure 2. Changes in time velocity integral of the diastolic coronary flow (Dtvi) and Dtvi \times HR after food intake in controls (upper panel) and in patients (lower panel). Dtvi and Dtvi \times HR increased in controls after food intake. In patients, Dtvi and Dtvi \times HR decreased after food intake. *p < 0.05, †p < 0.005 compared with the fasting state by the Wilcoxon signed rank test.
HR: $1,449.6 \pm 1,044.0 \text{ cm/min vs. } 1,273.4 \pm 1,000.9, p = 0.002$ (Figs. 2 and 3).

In six patients with successful percutaneous coronary interventions, the CBF pattern after food intake before intervention was similar to that of the whole patient group. However, the CBF pattern converted to that of the control group after intervention (Figs. 4 and 5).

**Effects of sham meal on coronary flow.** There were no significant changes in BP and HR after a sham meal. In addition, CBF did not change significantly after a sham meal (Figs. 6 and 7).

**Inter- and intra-observer variability.** Inter- and intra-observer variability was assessed in 10 of the controls and found to be 6.4% and 0.8%, respectively, for the measurement of Dtvi.

**DISCUSSION**

As the CBF dominates during the diastolic period, the CBF in one cardiac cycle can be represented by Dtvi multiplied by the cross-sectional area of the coronary artery. Assuming that the coronary artery has a constant cross-sectional area,
changes in Drvi represent changes in the CBF in one cardiac cycle. Therefore, changes in the CBF can be estimated from the product of Drvi and HR.

Postprandial hemodynamics. After food intake, splanchnic vascular beds dilate and total vascular resistance decreases (4,7). To maintain BP and to meet the metabolic demands of digestion, there is a compensatory increase in cardiac output and HR (8–12). Regarding the changes in BP, it is reported that mean and diastolic BP decrease (4,11) after food intake, and may even cause syncope in the elderly (13,14). However, several studies (2,5,15) did not show significant change in BP after food intake. In our study, postprandial hemodynamics both in the controls and in patients showed an increase in systolic BP, a decrease in diastolic BP, and an increase in HR after food intake.

Pathophysiologic mechanism of postprandial angina. Several mechanisms have been suggested for postprandial angina. Redistribution of blood from the coronary artery to the splanchnic artery, or exercising muscles in the case of exertional postprandial angina, were once proposed (6). However, these mechanisms have not been proven in humans (16). Increased myocardial oxygen demand, associated with an increase in HR and sympathetic nervous activity after food intake, is a commonly believed mechanism (2,17,18). However, Figureas et al. (19) showed that there is no change in the product of HR and systolic BP at the onset of ischemic electrocardiographic abnormalities and suggested decreased myocardial perfusion as a possible mechanism of postprandial angina. Later, these investigators showed that myocardial ischemia was not induced when the patients were paced to the same HR observed during postprandial angina (20) and suggested that other factors such as coronary vasoconstriction, rather than increased oxygen demand, might play a role in producing postprandial angina.

Recently, Baliga et al. (5) showed reduced myocardial blood flow in the stenotic artery territory after food intake with an increase in blood flow in the normal artery territory, by using positron emission tomography. They suggested that the redistribution of myocardial blood flow might be the mechanism of postprandial angina.

In our study, in contrast with the control group, CBF distal to significant stenosis in patients did not show postprandial surge in CBF after food intake; rather, the CBF was significantly decreased after food intake. This absence of postprandial surge distal to the significant stenosis is not likely to be a global phenomenon, because when the stenosis was relieved by intervention, the normal pattern of postprandial surge in CBF was restored. Therefore, we speculate that the CBF is redistributed to territory of the normal or insignificantly stenotic coronary artery.

Although our study included patients with multivessel disease, functionally significant stenosis based on the sestamibi SPECT was confined to the LAD, and the inclusion
of these patients would not affect the interpretation of our results.

Types of meals producing postprandial angina. The relationship between the components of a meal and the precipitation of postprandial angina is controversial. It has been proposed that postprandial angina is more likely to be precipitated by a fatty meal, which leads to postprandial endothelial dysfunction (21,22). However, other studies have suggested that a high-carbohydrate meal, rather than a fatty meal, is more likely to precipitate postprandial angina (11,23). In our study, we did not evaluate the effect of meal components. However, in contrast to a previous study (24), simple gastric distension by drinking water of the same volume as the standard meal did not affect the CBF, suggesting that a change in the CBF after food intake is not a vagally mediated response.

Study limitations. Because of the intrinsic limitation of the transthoracic Doppler echocardiographic evaluation of coronary flow, we could not measure the CBF in the right and left circumflex artery in our patients. Therefore, the pres-
ence of a “steal phenomenon” is postulated from the indirect evidence offered by the presence of postprandial surge in the CBF of healthy controls and of the restored normal pattern when stenosis is relieved. In addition, when estimating coronary blood flow, we neglected the flow during systole and assumed that the cross-sectional area of the coronary artery was constant during the study period.

We enrolled young, healthy volunteers as controls to minimize the possibility of their having coronary artery disease; therefore, age and gender ratio were not matched between the patient and control groups. Also, we did not limit the patient group to patients with postprandial angina.

**Conclusions.** Myocardial oxygen demand represented by the product of BP and HR increased after food intake. However, there was also a decrease in CBF distal to the significant stenosis, which suggests that steal phenomenon may play a role in the mechanism of postprandial angina.

![Figure 6](image-url)

*Figure 6.* Changes in time velocity integral of the diastolic flow velocity (Dtvi) and Dtvi × HR after sham feeding. No significant changes in Dtvi or Dtvi × HR were observed after sham feeding.

![Figure 7](image-url)

*Figure 7.* Coronary flow velocities in the fasting state and 15, 30, and 45 min after the sham meal. No significant changes in time velocity integral of the diastolic flow velocity occurred after a sham meal. Numbers in each tracing denote time velocity integral of the diastolic flow velocity.
REFERENCES