Phasic Coronary Flow Pattern and Flow Reserve in Patients With Left Bundle Branch Block and Normal Coronary Arteries

Emmanuel I. Skalidis, MD, George E. Kochiadakis, MD, Sophia I. Koukouraki, MD,* Fragiskos I. Parthenakis, MD, Nikolaos S. Karkavitsas, MD,* Panos E. Vardas, MD, PhD, FESC, FACC

Heraklion, Crete, Greece

OBJECTIVES

The purpose of this study was to determine whether scintigraphic myocardial perfusion defects in patients with left bundle branch block (LBBB) and normal coronary arteries are related to abnormalities in coronary flow velocity pattern and/or coronary flow reserve.

BACKGROUND

Septal or anteroseptal defects on exercise myocardial perfusion scintigraphy are common in patients with LBBB and normal coronary arteries.

METHODS

Thirteen patients (7 men, age 61 ± 8 years) with LBBB and normal coronary arteries underwent stress thallium-201 scintigraphy and cardiac catheterization. In all patients and in 11 control subjects coronary blood flow parameters were calculated from Doppler measurements of flow velocity in the left anterior descending coronary artery (LAD) before and after adenosine administration.

RESULTS

The time to maximum peak diastolic flow velocity was significantly longer both for the seven patients with (134 ± 19 ms) and for the six without (136 ± 7 ms) exercise perfusion defects than for controls (105 ± 12 ms, p < 0.05), whereas the acceleration was slower (170 ± 42, 279 ± 96 cm/s², respectively, p < 0.05). Coronary flow reserve in the patients with exercise perfusion defects (2.7 ± 0.3) was significantly lower than in those without (3.7 ± 0.5, p < 0.05) or in the control group (3.4 ± 0.5, p < 0.05).

CONCLUSIONS

Patients with LBBB have an impairment of early diastolic blood flow in the LAD due to an increase in early diastolic compressive resistance resulting from delayed ventricular relaxation. Furthermore, exercise scintigraphic perfusion defects in these patients are associated with a reduced coronary flow reserve, indicating abnormalities of microvascular function in the same vascular territory. (J Am Coll Cardiol 1999;33:1338–46) © 1999 by the American College of Cardiology

Left bundle branch block (LBBB) is a quite common disorder and is often associated with organic heart disease. Although the presence of LBBB was associated with a three- to fourfold increase in cumulative cardiovascular mortality in the Framingham study (1), patients with no clinically overt heart disease have an excellent two-year prognosis (2). Thus, it is important to determine whether patients with LBBB also have coronary artery disease or other organic heart disease.

Noninvasive evaluation of coronary artery disease in these patients has several limitations. Exercise-induced electrocardiographic (ECG) ST-segment changes are nonspecific in the presence of LBBB (3). Exercise myocardial perfusion scintigraphy would then appear to be a natural diagnostic choice in these patients. However, exercise perfusion scintigraphy is also limited because so-called false-positive perfusion defects occur frequently in patients with this conduction abnormality (4–6). Likewise, radionuclide ventriculography is hampered by the asynchronous contraction that these patients have at rest and that worsens with exercise (7). Pharmacologic coronary vasodilatation with intravenous (IV) dipyridamole (8–11) or adenosine (12,13) and pharmacologic stress with dobutamine (13) appear to be associated with higher specificity than that of exercise, but there are still false-positive results.

The mechanism of false-positive septal perfusion defects in patients with LBBB is not fully understood. Several hypotheses have been postulated, based on experimental animal studies (14,15), but no studies of this mechanism have been reported in humans.

The purpose of this study was to determine whether in patients with LBBB there are abnormalities in coronary flow velocity pattern and/or in coronary flow reserve that could be responsible for these findings.
Abbreviations and Acronyms

ANOVA = analysis of variance  
ECG = electrocardiographic  
IV = intravenous  
LAD = left anterior descending coronary artery  
LBBB = left bundle branch block

METHODS

Patients. The study included 16 patients with permanent and complete LBBB who consented to have stress thallium-201 scintigraphy and cardiac catheterization within two months. Left bundle branch block was defined according to standard ECG criteria. The following patient groups were excluded on clinical and echocardiographic grounds: patients with previous myocardial infarction, significant valvular disease, hypertension or left ventricular hypertrophy; patients with left ventricular ejection fraction <50%, total plasma cholesterol >220 mg/dl or diabetes mellitus. We also excluded extremely obese patients and women with large breasts. All cardioactive medications were continued.

Control group. Eleven patients who had coronary angiography for clinical indications and whose coronary arteries were free of stenotic lesions consented to have Doppler guide-wire measurement of coronary flow reserve. The same exclusion criteria were also applied to this group. All patients and controls gave their written informed consent to participation in the study. The study protocol was approved by the hospital’s Ethics Committee.

Stress protocol. All patients underwent a symptom-limited treadmill exercise test using the standard Bruce protocol. Blood pressure, heart rate and 12-lead ECG were recorded at 3-min intervals or when there was a clinical indication. Three millicuries of thallium were injected during peak stress, and the patient was encouraged to exercise for an additional 1 min. Imaging was performed as soon as possible after the end of exercise and 4 h later.

Patients with exercise perfusion defects in the left anterior descending coronary artery (LAD) region also underwent, one month later, a scintigraphic study under pharmacologic stress with dipyridamole. All had a 4-min IV infusion of 0.56 mg/kg dipyridamole. Cardiac rhythm was monitored continuously, and 12-lead ECG, blood pressure, and heart rate were obtained every 2 min during the test. Three minutes after the end of dipyridamole infusion, 3 mCi of thallium was administered and imaging was performed 3 min and 4 h later.

Thallium-201 single-photon emission computed tomography (SPECT). Thallium-201 SPECT imaging was performed with a dual-head SPECT gamma camera (Optima NX, General Electric, Milwaukee, Wisconsin) by use of a step-and-shoot approach every 6° over a 180° clockwise circular orbit beginning at a 45° right anterior oblique projection and ending at 45° left posterior. Filtered back-projection was performed using a Butterworth filter with a cutoff frequency of 0.4 cycles/pixel to reconstruct transverse tomograms of the left ventricle. Attenuation correction was not used. These images were further processed to obtain the short-axis and long-axis sections perpendicular to the cardiac axes.

The tomograms were divided into 13 segments for qualitative interpretation. Three short-axis slices (apex, midventricular, base) were divided into four regions. The apex was interpreted from the vertical long-axis view at the midventricular level. Perfusion was scored qualitatively by consensus of two experienced observers who were unaware of other patient data: 0 = severe perfusion defect; 1 = moderate perfusion defect; 2 = mild or equivocal perfusion defect; and 3 = normal perfusion. Defects in the short-axis slices were confirmed in the other two planes. A reversible defect was defined as a segment with a higher score on the rest images. The vascular territories were assigned as follows: anterior and apex to left anterior descending; lateral to left circumflex; and inferior to right coronary artery.

For quantitative assessment, polar mapping was performed as described previously (16). To assess the severity of the defect further, a region of interest was drawn on the abnormal segments. Counts in the septal region were quantified and normalized to the highest count region. A similar analysis was performed on the delayed images.

Coronary angiography. All patients underwent selective coronary angiography using 6F standard catheters and conventional views. On completion of diagnostic cardiac catheterization, the video record of the procedure was reviewed. Only patients whose coronary arteries were angiographically normal were enrolled in the study.

Coronary-flow velocity measurements. Immediately following coronary angiography the left and right coronary arteries (in random order) were selectively engaged with a diagnostic catheter. All patients received 80 IU/kg of IV heparin, and 200 μg intracoronary nitroglycerin was given every 30 min of the procedure to prevent catheter-induced coronary artery spasm and to avoid changes in coronary artery diameter. A 0.014-in. (0.036-cm), 15-MHz Doppler guide wire (FloWire, Cardiometrics, Mountain View, California) was advanced through the catheter to the proximal LAD, before the origin of the first septal branch, and then to the proximal right coronary artery. Baseline flow-velocity measurements were made at these positions once a stable Doppler signal was obtained. This was accomplished by means of torque adjustments. Frequency analysis of the Doppler signals was carried out in real time by fast Fourier transform using a velocimeter (FloMap, Cardiometrics, Mountain View, California). Once baseline flow-velocity data had been obtained, a bolus injection of intracoronary adenosine, 18 μg for the left and 12 μg for the right coronary artery, was given to obtain data during hyperemia. To confirm that maximal hyperemia had been achieved,
coronary blood flow velocity was recorded during administration of an additional larger dose of adenosine (4 \( \mu \)g larger than the initial dose).

Phasic coronary flow patterns along with simultaneous ECG and aortic pressure waveforms were displayed and recorded on videotape. Doppler velocity signals were analyzed using a special computer system. The envelope of the flow-velocity signal at baseline and at maximal hyperemia was traced by hand, and the following variables for the LAD were measured: 1) systolic coronary flow-velocity integral, defined as the area under the peak velocity curve during systolic coronary flow; 2) diastolic coronary flow-velocity integral, defined as the area under the peak velocity curve during diastolic coronary flow; 3) total coronary flow-velocity integral, defined as the sum of systolic and diastolic coronary flow-velocity integrals; 4) end-systolic peak coronary flow velocity, defined as the peak coronary flow velocity at the beginning of diastolic flow; 5) maximum (diastolic) peak coronary flow velocity; 6) time to maximum peak coronary flow velocity, measured from the onset of diastolic coronary flow; and 7) acceleration, defined as the slope of the line connecting the points on the Doppler tracing that represent the end-systolic peak coronary blood flow velocity and the maximum peak flow velocity. The average of three consecutive beats was used for quantitative analysis.

Coronary flow reserve was determined as the ratio of the time-averaged peak coronary flow velocity after adenosine administration to the time-averaged peak coronary flow velocity at baseline, for both left and right coronary arteries. The data showing the maximum increase in coronary flow velocities after adenosine administration were used for the determination of coronary flow reserve and for the calculation of the above variables at maximal hyperemia.

**Statistical analysis.** Data are expressed as mean values ± SD. Two-way repeated measures analysis of variance (ANOVA) was used to assess drug (adenosine-induced maximal hyperemia), group and interaction effects. A one-way ANOVA was used for all other comparisons among the three groups. The correlation between maximum peak velocity and acceleration was assessed by simple linear regression analysis.

A probability value of less than 0.05 was considered as statistically significant.

**RESULTS**

Of the 16 patients initially included in the study two had coronary artery disease and one had poor quality recordings; these patients were excluded from the final analysis.

For the remaining 13 patients (7 men) the mean age was 61 ± 8 years. Two of them had typical angina and eight had nontypical chest pain syndrome. Seven patients were taking nitrates regularly or intermittently, two were taking beta-blockers and two calcium channel antagonists.

In the control group, which included six men, the mean age was 59 ± 8 years. Seven of them had nontypical chest pain syndrome with a negative or nondiagnostic exercise ECG. The remaining four were asymptomatic and had cardiac catheterization for episodes of nonsustained ventricular tachycardia. Four patients were taking nitrates regularly or intermittently, two were taking beta-blockers and one amiodarone.

**Exercise thallium-201 SPECT.** In seven patients qualitative interpretation showed perfusion defects in the LAD area (Group I). One of these also had a defect in the right coronary artery area. The septal region was involved in all cases. In addition, extension of the defects to the anterior region was observed in three and to the apex in four patients (Table 1). Another patient with a defect in the right coronary artery area and five patients with no perfusion...
Table 2. Doppler and Other Parameters Recorded at Baseline and at Maximum Hyperemia in Patients With Left Bundle Branch Block With (Group I) and Without (Group II) Exercise Scintigraphic Perfusion Defects and in Controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I</th>
<th>Group II</th>
<th>Controls</th>
<th>Group I</th>
<th>Group II</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>74 ± 16</td>
<td>71 ± 12</td>
<td>70 ± 14</td>
<td>74 ± 14</td>
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<td>70 ± 12</td>
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<tr>
<td>SBP (mm Hg)</td>
<td>129 ± 15</td>
<td>133 ± 12</td>
<td>132 ± 17</td>
<td>129 ± 12</td>
<td>135 ± 11</td>
<td>130 ± 16</td>
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<tr>
<td>DBP (mm Hg)</td>
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<td>67 ± 11</td>
<td>73 ± 10</td>
<td>77 ± 11</td>
<td>67 ± 9</td>
<td>72 ± 9</td>
</tr>
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<td>ESPV (cm/s)*</td>
<td>15.8 ± 10.2</td>
<td>12.3 ± 9.2</td>
<td>8.2 ± 4.7</td>
<td>40.4 ± 28.5</td>
<td>36.1 ± 12.5</td>
<td>23.7 ± 13.4</td>
</tr>
<tr>
<td>MPV (cm/s)*</td>
<td>41.4 ± 18.4</td>
<td>35.8 ± 13.8</td>
<td>35.2 ± 12.4</td>
<td>100.2 ± 47.1</td>
<td>105.1 ± 36.6</td>
<td>106.2 ± 38.1</td>
</tr>
<tr>
<td>FVI1 (cm/min)*</td>
<td>297 ± 110</td>
<td>294 ± 88</td>
<td>253 ± 84</td>
<td>1023 ± 543</td>
<td>1242 ± 436</td>
<td>909 ± 457</td>
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<tr>
<td>FI1d (cm/min)*</td>
<td>1181 ± 473</td>
<td>960 ± 409</td>
<td>970 ± 362</td>
<td>3168 ± 1300</td>
<td>3362 ± 1398</td>
<td>2901 ± 1451</td>
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<tr>
<td>FVI1t (ms/min)*</td>
<td>1478 ± 578</td>
<td>1251 ± 462</td>
<td>1223 ± 431</td>
<td>4191 ± 1733</td>
<td>4604 ± 1759</td>
<td>3803 ± 1851</td>
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<tr>
<td>TMP (ms)†</td>
<td>134 ± 19</td>
<td>136 ± 7</td>
<td>105 ± 12</td>
<td>134 ± 26</td>
<td>133 ± 12</td>
<td>104 ± 15</td>
</tr>
<tr>
<td>Acc (cm/s²)**†</td>
<td>170 ± 54</td>
<td>186 ± 42</td>
<td>279 ± 96</td>
<td>463 ± 178</td>
<td>523 ± 210</td>
<td>807 ± 306</td>
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</tbody>
</table>

*Significant drug effect. †Significant group effect at both baseline and hyperemia.

**Acc = acceleration; DPB = diastolic blood pressure; ESPV = end systolic peak flow velocity; FVI1 = flow-velocity integral (s/d/t systolic/diastolic/total); HR = heart rate; MPV = maximum peak flow velocity; SBP = systolic blood pressure; TMPV = time to maximum peak flow velocity.

defects made up Group II (normal perfusion scintigraphy in the LAD).

The perfusion defects were completely or partially reversible in all patients.

There were no statistically significant differences between patients with and without perfusion defects in relation to peak heart rate (148 ± 9 vs. 140 ± 9 beats/min, p = NS) achieved during exercise.

Chest pain was the reason for exercise termination in two patients from Group I and in two patients from Group II. Fatigue and/or dyspnea were the reason in the others.

By quantitative analysis, the polar map confirmed the qualitative classification in all patients. Because the septum was involved in all cases, this was chosen as the region of interest: the mean counts in the septum in Group I during stress were 59 ± 7% of normal in Group I and 81 ± 7% in Group II (p < 0.05). On delayed imaging, the mean counts increased to 80 ± 8% of normal in Group I (p < 0.05 vs. stress) but did not change in Group II (79 ± 9%).

Dipyridamole thallium-201 SPECT. None of the seven patients who underwent pharmacologic stress had a perfusion defect (Table 1). The maximum heart rate during the pharmacologic stress was 91 ± 12 beats/min, significantly lower than that achieved during exercise stress (148 ± 9 beats/min, p < 0.05).

Coronary flow-velocity measurements. LEFT CORONARY ARTERY. The Doppler and other parameters recorded at baseline and at maximum hyperemia are given in Table 2. Group and drug effects are shown in the same table.

TIME TO MAXIMUM PEAK FLOW VELOCITY. There was a significant group effect (p = 0.001) but no significant drug effect. Control subjects had lower values than did Group I and Group II patients both at baseline and during hyperemia (Fig. 1). No significant difference existed between Group I and Group II patients.

ACCELERATION. There was a significant group effect both at baseline and during maximal hyperemia (p = 0.016). Control subjects had faster acceleration than did Group I and Group II patients. There was also a significant drug effect (0.001), but this was not the same in the three groups (significant interaction p = 0.04). Again, no significant difference existed between Group I and Group II patients.

There was a significant correlation between maximum peak flow velocity and acceleration for both controls (R² = 93% at baseline, 89% at hyperemia) and patients with LBBB (R² = 82% at baseline, 81% at hyperemia). In this instance Group I and Group II patients were considered as one population with LBBB due to the small number of patients in each group. Furthermore, there was a significant difference in the slope of the regression line for these values, which at baseline (Fig. 2A) was 7.2 in the control group versus 2.4 in the patients with LBBB (p < 0.05) and at maximal hyperemia (Fig. 2B) was 7 in the control group versus 3.6 in the LBBB patients.

Figure 1. Time to maximum peak flow velocity (Time to MPV) for patients with left bundle branch block with (Group I) and without (Group II) scintigraphic perfusion defects, and for controls. Individual data points: tagged circles indicate where values from two or more patients almost coincide.
Coronary flow reserve in patients with exercise perfusion defects (Group I) was 2.7 ± 0.3, significantly lower than in patients without defects (Group II: 3.7 ± 0.5, p < 0.05) or the control group (Control: 3.4 ± 0.5, p < 0.05) (Fig. 3). There were no statistically significant differences in coronary flow reserve between Group II and the controls.

Right coronary artery. Coronary flow reserve was 3.9 ± 0.9 in Group I, 3.7 ± 0.5 in Group II, and 3.9 ± 0.8 in the controls; the differences between these values were not statistically significant.

Coronary flow reserve in the two patients with an exercise inferior perfusion defect was 3.4 and 4.2, but the small number of patients makes any comparisons doubtful.

Left vs. right coronary artery. Coronary flow reserve was the same in the left and right coronary arteries in the control group (3.4 ± 0.5 vs. 3.9 ± 0.8, p = NS).

In Group I patients, the coronary flow reserve in the LAD (2.7 ± 0.3) was significantly lower than that in the right coronary artery in Group I (3.9 ± 0.9, p < 0.05), Group II (3.7 ± 0.5, p < 0.05) and controls (3.9 ± 0.8, p < 0.05).

**DISCUSSION**

This study is the first to evaluate coronary flow velocity pattern and coronary flow reserve in patients with LBBB and normal coronary arteries. We found that in these patients there is an impairment of early diastolic coronary blood flow in the LAD, as expressed by longer time and slower acceleration of flow to reach maximum peak flow velocity in this time period. In addition, patients with LBBB and exercise perfusion defects in the LAD territory have a reduced coronary flow reserve to adenosine in this area.

**Normal coronary flow-velocity pattern.** The flow in the LAD shows a phasic pattern, with the greatest amount of flow occurring during the diastolic period (17,18). This pattern is thought to be caused by the transmural compression of the intramyocardial vessels during systole and release of the compressive force during diastole.

**Coronary flow-velocity pattern in LBBB.** In patients with LBBB there is an asynchronous ventricular contraction with contraction of the septum in the late systolic or early diastolic period.

This is supported by the findings of Ono et al. (14), who showed that in experimental dogs after the induction of LBBB the pattern of the septal intramyocardial pressure changed and the peak intramyocardial pressure moved from the early or midsystolic phase to the late systolic or early diastolic phase (Fig. 4). Therefore, release of the compressive force in the septum vessels during diastole is also delayed.

Because first, there are qualitative similarities between the phasic flow in the large epicardial coronary arteries and the flow in the intramyocardial septal artery, as Carew and Covell (19) reported, and second, LAD flow includes septal...
flow, the delayed septal relaxation restricts the blood flow in this artery during early diastole. This is one possible mechanism that could cause the maximum flow in the LAD to be achieved with slower acceleration and over a significantly longer time than normal. This pattern is shown in Figure 5, which compares typical Doppler coronary flow-velocity recordings from patients with LBBB (Groups I and II) with one from the control group, both at baseline and at maximal hyperemia. Figure 4 shows a similar pattern to the baseline recordings, although the original investigators did not comment on this. As Figure 2 shows, this effect is maintained irrespectively of the value of maximum peak flow velocity.

Masuyama et al. (20) showed that the time to maximum peak flow velocity is longer and the acceleration slower in patients with abnormal ventricular relaxation due to cardiomyopathy. This was not the case in our study because of our exclusion criteria, although primary abnormal relaxation remains a possible explanation. Recently, Sadaniantz et al. (21) showed that LBBB is associated with significant alterations in diastolic filling patterns, but these investigators excluded patients with exercise perfusion defects. We do not yet have full data about ventricular relaxation, even though preliminary findings show an abnormal relaxation in these patients. Clearly, we need more information to determine whether the impairment of early diastolic coronary flow is due to abnormal septal relaxation only or to a more diffuse abnormal ventricular relaxation.

**Coronary flow reserve in LBBB.** Coronary flow reserve to adenosine in the LAD in our patients with LBBB and exercise perfusion defects in the same territory were significantly lower than in patients without these defects or this conduction abnormality. This implies that in some of these patients there is impairment of coronary microvascular function in the region of the LAD. In the right coronary artery, coronary flow reserve was not different from the control values.

**Stress thallium-201 SPECT.** Cumulative results indicate that septal or anteroseptal perfusion defects on exercise perfusion scintigraphy were present in 73% of patients with LBBB, whereas significant LAD stenosis was detected in only 42% (10). Several hypotheses have been suggested to explain the underlying mechanism causing the high proportion of false-positive perfusion defects: 1) In LBBB the septum contracts late in systole at a time when the ejection is already in progress. At that time the outflow resistance is lower and, as a consequence of coronary autoregulation (22), perfusion is reduced; 2) small-vessel disease associated with fibrodegenerative changes may cause both the conduction abnormality and the exercise perfusion defects (23,24), but no previous studies have assessed this; and 3) the abnormal perfusion is a direct result of the restricted blood flow due to the delayed septal contraction (14,24).

Joye et al. (25) showed that, in patients with intermediate coronary artery stenosis, Doppler guide-wire measurements of coronary flow reserve were 95% concordant with stress SPECT thallium-201 results, with a cutoff value for coronary flow reserve of 2. Because our patients with perfusion defects had a coronary flow reserve to adenosine of 2.7 ± 0.3, this cutoff value, by itself, does not explain the exercise perfusion defects we observed but is consistent with the absence of perfusion defects on scintigraphy under pharmacologic stress with dipyridamole. Consequently, a reduced
coronary flow reserve resulting from microvascular disease could be only partially responsible for the exercise scintigraphic findings.

In fact, however, the coronary flow response to adenosine seems to be quite different from the response to exercise. Adenosine exploits the coronary vasodilatory flow reserve uniformly, without affecting heart rate, and is thus unable to reveal underlying perfusion differences in patients with LBBB. In contrast, exercise, by decreasing the diastolic period, exacerbates any perfusion differences that are due to the impairment of early diastolic flow, as the contribution of early diastolic flow to total diastolic coronary flow becomes more important during tachycardia.

In consequence, exercise tachycardia may lead to a more significant restriction of flow in the LAD than might be expected given the values of coronary flow reserve to adenosine or the response to dipyridamole, which has a much smaller effect on heart rate than does exercise.

In summary, the reduced coronary flow reserve and the impaired early diastolic flow in the LAD combine to produce a diminution in coronary blood flow, which is sufficient to create perfusion defects on exercise scintigraphy.

It is possible that both the conduction abnormality and the reduced coronary flow reserve are the result of the same fibrodegenerative process, but because it is impractical to carry out serial scintigraphic and flow-reserve evaluation, the time sequence is unclear.

**Previous studies.** Both Hirzel et al. (15) and Ono et al. (14) found that, in dogs, the induction of LBBB by right ventricular pacing itself may reduce regional myocardial blood flow in the septum, as peak intramyocardial pressure was seen in the late systolic or early diastolic phase. This was observed at a pacing rate of $196 \pm 16$ beats/min. Thus, the delayed compression of the septal arteries, as a consequence of asynchronous septal contraction due to aberrant and delayed depolarization in LBBB, causes impairment of septal blood flow, especially during tachycardia. This is in concordance with our findings from patients with LBBB.

Ono et al. (14) also found that neither lactate extraction rate nor lactate production changed significantly after induction of LBBB in experimental animals and concluded that reduced myocardial septal blood flow is not necessarily an indication of septal ischemia, but may be caused by hypoperfusion due to autoregulation resulting from the lower demands of the septum. This is in conflict with our findings, where the reduced coronary flow reserve to adenosine (the response to which is independent of myocardial demands) showed an impairment of microvascular function, suggesting that true ischemia was the cause of the perfusion defects. However, the former investigators performed their measurements in the acute phase of LBBB that was induced experimentally by right ventricular pacing. Thus, they could only detect acute functional changes resulting from pacing in a healthy substrate. This, in conjunction with the fact that relaxation times are significantly shorter during pacing than in true LBBB (26), means that the reduction of septal blood flow would be less severe.

Patients with abnormal ventricular relaxation have decreased coronary flow in early diastole at rest. During tachycardia, total coronary flow increases. However, the increase is smaller than in patients with normal ventricular relaxation because diastolic coronary flow decreases rather than increases (20). The similar early diastolic flow abnormality seen in our patients supports our hypothesis regarding coronary flow regulation during exercise tachycardia.

Vaduganathan et al. (13) found that false-positive perfusion defects in the septum extended to the anterior wall and the apex in about 60% of cases, which is concordant with our scintigraphic findings.

Sugihara et al. (27) found that rest perfusion defects in the septal region on nongated images can be eliminated with ECG-gated technetium-99m-sestamibi SPECT, particularly with end-diastolic images, suggesting that these perfusion defects are a result of reduced wall thickening rather than actual hypoperfusion at rest. We did not find any difference in the time-averaged peak coronary flow velocities at baseline, although in the absence of knowledge of coronary artery dimensions inferences regarding perfusion cannot be certain. However, the patient population in our study seems to have been different from that of Sugihara et al. (27) as the septal count ratio was $80 \pm 9\%$ of normal in our study and $72 \pm 9\%$ in the latter. As those researchers stated, ECG-gated SPECT during exercise will be necessary to clarify to what extent reduced septal thickening contributes to the pathogenesis of exercise perfusion defects.

**Study limitations.** In the present study, coronary blood flow responses were assessed by using intracoronary Doppler measurement of coronary flow velocity. Although extensive animal studies have validated the accuracy of Doppler measurements in the assessment of changes in coronary flow (28,29), the technique by itself is not capable of measuring absolute myocardial perfusion. Also, we measured coronary artery flow velocity and flow reserve in the LAD, rather than the septum. However, by positioning the tip of the Doppler wire proximal to the first septal branch, we included the septal flow in our measurements. Moreover, the range of the perfusion defects we observed suggests that the disease process is usually related with the entire LAD territory and is not restricted to the septum.

We have no complete data on coronary flow velocity or lactate production during tachycardia to confirm our hypotheses, which are based on the coronary flow-velocity pattern at rest. During the catheterization of the last patient (Patient 11 in Table 1) we performed atrial pacing to control heart rate. After measurement of coronary flow reserve at 100 beats/min, which was the heart rate during dipyridamole scintigraphy, we did the same at 140 beats/min. As Figure 6 shows, the reduction in cycle length at the higher rate is at the expense of diastolic flow. Because early
diastolic flow did not increase further, time-averaged peak flow velocity diminished and, as a consequence, actual coronary flow reserve fell from 2.4 at 100 beats/min to 1.9 at 140 beats/min. Although this is a single-patient observation, it is in support of our hypothesis.

Conclusions. The findings of this study show that patients with LBBB have an impairment of early diastolic blood flow in the LAD. They also suggest that the exercise scintigraphic perfusion defects, which are commonly observed in these patients, are associated with a reduced coronary flow reserve in the area supplied by that coronary artery. However, studies of larger patient populations during tachycardia and measurement of lactate production will be needed to validate the hypotheses we present here.

Acknowledgments
The authors would like to thank Mr. Gregory Chlouverakis for the statistical analysis and Mr. Philip Lees for assistance with critical revision of the text.

Reprint requests and correspondence: Prof. Panos E. Vardas, Cardiology Department, Heraklion University Hospital, P.O. Box 1352 Stavrakia, GR 711 10 Heraklion, Crete, Greece. E-mail: cardio@danae.med.uoc.gr.

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