Phasic Coronary Blood Flow Velocity Pattern and Flow Reserve in the Atrium: Regulation of Left Atrial Myocardial Perfusion

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OBJECTIVES
The purpose of this study was to assess rest and stress atrial coronary blood flow (CBF) velocity and flow reserve.

BACKGROUND
Because of the limitations of the methods used until now for assessing myocardial perfusion (MP) in the small mass of atrial tissue, data are lacking for human atrial MP.

METHODS
Seventeen patients with suitable coronary anatomy underwent CBF velocity measurements with the use of a Doppler guide wire in the proximal left circumflex coronary artery (LCx) and left atrial circumflex branch (LACB), at baseline and after adenosine administration. All measurements were performed at resting heart rate and at 100 and 120 beats/min.

RESULTS
Coronary blood flow velocity in the LACB showed a predominant systolic pattern in contrast to the diastolic pattern of the LCx. There was a disproportionate increase in baseline time-averaged peak coronary flow velocity (cm/s) between the LACB and LCx during the two levels of pacing-induced stress (16.8 ± 5.5 vs. 16.2 ± 5.1 at rest; 22.9 ± 7.9 vs. 18.4 ± 5.2 at 100 beats/min; and 27.1 ± 8.0 vs. 20.4 ± 5.1 at 120 beats/min; significant interaction, p < 0.001), but there were no significant differences in coronary flow reserve (CFR).

CONCLUSIONS
Coronary blood flow in the left atrium is out of phase with that in the ventricular myocardium, showing a predominant systolic pattern. Although atrial and ventricular CFR show no significant differences at rest and with two levels of stress, the disproportionate increase in atrial blood flow velocity during stress indicates a peculiarity of atrial perfusion regulation. (J Am Coll Cardiol 2003;41:674–80) © 2003 by the American College of Cardiology Foundation

The regulation and transmural distribution of coronary blood flow (CBF) in the human left ventricle (LV) have been extensively studied in health and disease. However, what little is known about atrial myocardial perfusion (MP) (1,2) and CBF regulation in the atria (3,4) is from experimental animal studies. A major reason for this gap in our knowledge is that, given the spatial resolution of gamma cameras, the smaller mass of atrial compared with ventricular tissue does not allow the detection of atrial perfusion. In addition, interest in the functional role of the atria has been overshadowed by studies of ventricular function.

Because of the double atrial function (as a conduit and as a booster pump) and the marked disparity between atrial and ventricular mechanical work, the atrial CBF requirements and CBF regulation are not known and are difficult to predict.

Accordingly, the purpose of our study was to identify potential differences in phasic CBF velocity pattern and coronary flow reserve (CFR) between atrial and ventricular MP.

METHODS
Patients. The study included 26 patients with suitable coronary anatomy who consented to undergo functional assessment of their coronary circulation after completion of programmed routine cardiac catheterization.

Suitable coronary anatomy means that the patients had a left atrial circumflex branch (LACB) at least 1 mm in diameter, originating without an obtuse angle from the proximal or mid left circumflex coronary artery (LCx). An LACB was defined as any branch that originated to the left of the LCx and the coronary sinus, in the right anterior oblique view.

The following patient groups were excluded: patients with a rhythm other than sinus rhythm, stenotic coronary artery lesions of any severity, previous myocardial infarction, significant valvular disease, electrocardiographic indications of LV hypertrophy, and LV ejection fraction <50%.

All patients gave their written, informed consent to participate in the study. The study protocol was approved by the hospital's Ethics Committee.

Coronary flow velocity measurements. 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.

The left coronary artery was selectively engaged with a diagnostic catheter. A 0.036-cm (0.014-in), 15-MHz Doppler guide wire (Jomed FloWire) was advanced through the catheter to the proximal LCx and LACB. Frequency analysis of the Doppler signals was carried out in real time by fast Fourier transform using a
velocimeter (Jometrics FloMap, Jomed, Sweden). Once baseline flow velocity data had been obtained, 18 μg intracoronary adenosine was given to obtain data during hyperemia.

The following variables were measured: 1) systolic flow velocity integral (FVI), defined as the area under the peak velocity curve during systolic CBF; 2) diastolic FVI, defined as the area under the peak velocity curve during diastolic CBF; 3) total FVI, defined as the sum of systolic and diastolic FVI; and 4) diastolic to systolic flow velocity integral ratio (DSVIR), defined as the ratio of diastolic to systolic FVI.

The CFR was determined as the ratio of time-averaged peak coronary flow velocity (APV) at maximal hyperemia to APV at baseline.

In each artery, all measurements were made at resting heart rate (HR) and after at least 5 min of pacing at 100 and 120 beats/min. This was accomplished by right atrial appendage pacing via a temporary pacing lead. Pretreatment and measurements were performed as previously described (5).

Statistical analysis. Data are expressed as the mean value ± SD. A repeated measures analysis of variance model with intra-subject factors pertaining to the artery (at two levels: LACB and LCx) and HR (at three levels: resting and 100 and 120 beats/min) was used to assess main and interaction effects on the various flow variables mentioned previously. The Huynh-Feldt epsilon adjustment on the degrees of freedom was used when significant departures from sphericity in the variance–covariance matrix were observed. Comparisons between subsequent levels of HR were accomplished with a repeated contrast. A p value <0.05 was considered statistically significant.

RESULTS

Of the 26 patients initially included in the study, 4 had poor-quality recordings, and in 5, the wire could not be selectively positioned in the LACB; these patients were excluded from the final analysis.

For the remaining 17 patients (12 men), the mean age was 64 ± 8 years. Fourteen of them were current or ex-smokers, five had arterial hypertension, six had dyslipidemia, and two had diabetes mellitus. No complications were noted from Doppler wire advancement to the LACB (Fig. 1).

Arterial blood pressure. Systolic and diastolic blood pressures recorded at resting HR and at 100 and 120 beats/min, both at baseline and maximal hyperemia, are given in Tables 1 and 2. Although there were no significant differences in systolic blood pressure as a result of HR augmentation, there was a statistically significant increase in diastolic blood pressure at a higher HR.

Coronary flow velocity measurements. LCx. The Doppler and other parameters recorded at resting HR (70 ± 11 beats/min) and at 100 and 120 beats/min, both at baseline and maximum hyperemia, are given in Tables 1 and 2, respectively. The HR, artery, and interaction effects are shown in these same tables. The CFR showed a gradual and statistically significant decrease with the increase in HR (3.0 ± 0.7 at resting HR; 2.6 ± 0.6 at 100 beats/min; and 2.2 ± 0.5 at 120 beats/min; p < 0.05).

LACB. The Doppler and other parameters recorded at resting HR (68 ± 10 beats/min) and at 100 and 120 beats/min, both at baseline and maximum hyperemia, are given in Tables 1 and 2, respectively. The HR, artery, and interaction effects are shown in these same tables. Percentage differences in APV between pacing and resting HR at baseline and maximal hyperemia are shown in Table 3. The CFR showed a gradual and statistically significant decrease with the increase in HR (3.0 ± 0.7 at resting HR; 2.6 ± 0.6 at 100 beats/min; and 2.2 ± 0.5 at 120 beats/min; p < 0.05).
Table 1. Doppler and Other Parameters Recorded at Baseline From the LACB and LCx

| Parameter | LACB | | | LCx | | | | |
|-----------|-----|---|---|-----|---|---|---|
| Rest | 100 beats/min | 120 beats/min | Rest | 100 beats/min | 120 beats/min |
| SBP (mm Hg) | 128 ± 17 | 130 ± 13 | 130 ± 16 | 127 ± 16 | 131 ± 12 | 129 ± 15 |
| DBP (mm Hg)* | 69 ± 13 | 73 ± 7 | 77 ± 8 | 69 ± 12 | 74 ± 7 | 76 ± 7 |
| FVIs (cm/min)†‡ | 549 ± 187 | 823 ± 371 | 960 ± 282 | 299 ± 98 | 388 ± 151 | 342 ± 188 |
| FVId (cm/min) † | 453 ± 171 | 554 ± 165 | 669 ± 254 | 672 ± 243 | 718 ± 242 | 879 ± 229 |
| DSVIR† | 0.84 ± 0.24 | 0.73 ± 0.20 | 0.71 ± 0.21 | 2.36 ± 0.82 | 2.11 ± 0.99 | 3.14 ± 1.64 |
| FVIt (cm/min) †‡ | 1,003 ± 325 | 1,377 ± 483 | 1,628 ± 478 | 971 ± 304 | 1,106 ± 311 | 1,221 ± 306 |
| FVIs/FVIt (%) | 55 ± 7 | 58 ± 8 | 59 ± 7 | 31 ± 7 | 35 ± 9 | 27 ± 10 |
| APV (cm/s) †‡ | 16.5 ± 5.5 | 22.9 ± 7.9 | 27.1 ± 8.0 | 16.2 ± 5.1 | 18.4 ± 5.2 | 20.4 ± 5.1 |

*Significant heart rate effect. †Significant artery effect. ‡Significant interaction. Data are presented as the mean value ± SD.

APV = time-averaged peak flow velocity; DBP = diastolic blood pressure; DSVIR = diastolic to systolic flow velocity integral ratio; FVI = flow velocity integral (s/dt) = systolic/diastolic total; LACB = left atrial circumflex branch; LCx = left circumflex coronary artery; SBP = systolic blood pressure.

Table 2. Doppler and Other Parameters Recorded at Maximum Hyperemia From the LACB and LCx

| Parameter | LACB | | | LCx | | | | |
|-----------|-----|---|---|-----|---|---|---|
| Rest | 100 beats/min | 120 beats/min | Rest | 100 beats/min | 120 beats/min |
| SBP (mm Hg) | 127 ± 15 | 131 ± 15 | 131 ± 14 | 129 ± 15 | 131 ± 13 | 131 ± 12 |
| DBP (mm Hg)* | 67 ± 10 | 72 ± 7 | 76 ± 8 | 787 ± 263 | 938 ± 419 | 733 ± 244 |
| FVIs (cm/min)†‡ | 1,410 ± 554 | 1,900 ± 686 | 1,871 ± 546 | 2,040 ± 743 | 1,858 ± 601 | 1,959 ± 679 |
| FVId (cm/min) † | 1,360 ± 342 | 1,102 ± 325 | 1,177 ± 427 | 2,640 ± 57 | 2,19 ± 0.67 | 2,74 ± 0.55 |
| DSVIR† | 1,087 ± 0.56 | 0.61 ± 0.18 | 0.65 ± 0.23 | 2,827 ± 959 | 2,796 ± 957 | 2,691 ± 869 |
| FVIt (cm/min) †‡ | 2,771 ± 788 | 3,002 ± 914 | 3,048 ± 841 | 28 ± 5 | 33 ± 7 | 27 ± 5 |
| FVIs/FVIt (%) | 51 ± 11 | 63 ± 6 | 62 ± 8 | 47.2 ± 16.0 | 46.6 ± 15.9 | 44.7 ± 14.5 |
| APV (cm/s) †‡ | 46.3 ± 13.2 | 50.1 ± 15.3 | 50.8 ± 14.0 | 3.0 ± 0.7 | 2.6 ± 0.6 | 2.2 ± 0.5 |
| CFR* | 2.8 ± 0.5 | 2.2 ± 0.3 | 1.9 ± 0.3 | 2.8 ± 0.5 | 2.6 ± 0.6 | 2.2 ± 0.5 |

*Significant heart rate effect. †Significant artery effect. ‡Significant interaction. Data are presented as the mean value ± SD.

CFR = coronary flow reserve; other abbreviations as in Table 1.

DISCUSSION

This study is the first to evaluate the phasic CBF velocity pattern and CFR in the arteries supplying the human atrial myocardium, as well as atrial CBF regulation under different energy requirements.

We found that the CBF of the atrium is out of phase with that of the ventricular myocardium, showing a predominant systolic pattern. In addition, there was a disproportionate increase in atrial compared with ventricular CBF velocity during stress, but no significant differences in CFR between the atrial and ventricular myocardium, either at rest or under different levels of stress.

Coronary flow velocity pattern in the atrium. Flow in the LV myocardium shows a phasic pattern, with the greatest amount of flow occurring during the diastolic period (6,7).

According to our findings, the CBF waveform in the atria is out of phase with that of the ventricular myocardium, both at baseline and maximal hyperemia, and is similar to the pattern of arterial pressure (Fig. 4 and 5). This phase opposition is not surprising, because during the ventricular systolic period, the left atrium acts as a reservoir at low pressures, not capable of impeding atrial CBF. Thus, the contribution of systolic to total CBF (FVIs/FVIt) is 27% to 35% for the ventricular myocardium and 51% to 63% for the atrial myocardium (Tables 1 and 2).

Atrial CBF is also characterized by a small diastolic peak and a large presystolic peak, with flow decreasing across systole. Peak LACB flow occurs nearly consistently with the aortic upstroke, where, of course, the LCx flow is at or near its minimum or falling (Fig. 4 and 5). The small diastolic peak in LACB flow occurs simultaneously with a transient decrease (atrial coves) in the flow of the LCx (8,9).

Diastolic abnormalities of the LV with profound effects on left atrial pressure could affect the perfusion pressure and might modify the CBF velocity pattern. Figure 6 shows...
Table 3. Percentage Differences (Δ) in Time-Averaged Peak Coronary Flow Velocity Between Pacing and Rest Heart Rate, for the Left Atrial Circumflex Branch and Left Circumflex Coronary Artery

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<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Maximal Hyperemia</th>
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<tbody>
<tr>
<td></td>
<td>Δ_{100-R} %</td>
<td>Δ_{120-R} %</td>
</tr>
<tr>
<td>LACB</td>
<td>37 ± 20%</td>
<td>66 ± 34%</td>
</tr>
<tr>
<td>LCx</td>
<td>15 ± 13%</td>
<td>29 ± 24%</td>
</tr>
</tbody>
</table>

Data are presented as the mean value ± SD.

Δ_{100-R} % = percentage difference between 100 beats/min and rest heart rate; Δ_{120-R} % = percentage difference between 120 beats/min and rest heart rate; LACB = left atrial circumflex branch; LCx = left circumflex coronary artery.

simultaneous recording of the pulmonary capillary wedge pressure and atrial CBF velocity.

CFR in the atrium. At resting HR, there were no significant differences in CFR between the LACB and LCx.

During stress (in our case, pacing tachycardia), baseline APV was significantly increased at each level of HR augmentation, but in different steps (Table 3 and Fig. 2A).

The greater proportional increase in atrial compared with ventricular CBF, although surprising, could be related to large differences in the wall stress between the two cardiac chambers. In addition, intrinsic characteristics of atrial myocytes may be the underlying cause for this disparity, as it is known that oxygen extraction in a dog’s atria is about half that of the ventricle (10).

The APV at maximal hyperemia changed in different directions in the two arteries, as a result of increased HR. Thus, LACB flow showed an increase, and LCx flow showed a decrease (Table 3 and Fig. 2B). Although these changes were not significant at 100 beats/min, they were statistically significant at 120 beats/min.

Although the exact mechanism is unclear, the final result of the aforementioned changes in baseline and maximal hyperemia CBF during stress is to keep CFR similar in the two arteries, although this is achieved by different means.

Consequently, in the case of a flow-limiting stenosis in the proximal LCx, one would expect a reduction of maximal flow at least, to the same degree in the two arteries. In that case, because of the disproportionate increase in atrial compared with ventricular CBF during stress, for any given HR (stress), the flow in the LACB will approach the maximal flow more closely, and thus the calculated atrial CFR will be lower than the ventricular. Thus, earlier exhaustion of CFR in the LACB compared with the LCx may be the final result.

Previous studies. Small arteries on the left atrial surface from open-chest dogs, in a study by Kajiya et al. (1), showed phasic CBF velocity characteristics at rest similar to those observed in our population, but no data were provided for stress.

During stress, in three studies by Manohar et al. (3) and Bauman et al. (2, 4), it was found that atrial CBF increased in horses and dogs, respectively, but the authors did not observe any significant differences between the atria and ventricles in the CFR. Nevertheless, careful observation of the published data from Bauman et al. (2, 4) reveals a disproportionate increase in atrial compared with ventricular CBF during stress, although this was ignored and not discussed. In addition, CBF at maximal hyperemia was assessed by adenosine infusion with the experimental animals at rest but not under stress (as in our study). Consequently, any effect of HR augmentation on CBF was not taken into account.

We also observed both an increase in atrial CBF and a similar CFR when comparing the atria and ventricles. However, the finding of a disproportionate increase in atrial compared with ventricular MP during stress runs counter to the concept of uniform regulation, rather indicating different mechanisms for atrial and ventricular MP regulation.

A reduction of total FVI at maximal hyperemia with increasing HR in the arteries supplying the ventricular myocardium has been reported in two other studies (11, 12), consistent with our data.
Figure 3. Mean values with 95% confidence intervals (CIs) of coronary flow reserve (CFR) in the left atrial circumflex branch (LACB) and left circumflex coronary artery (LCx) at rest heart rate and at 100 and 120 bpm.

Figure 4. The left atrial circumflex branch (LACB) and left circumflex coronary artery (LCx) baseline coronary flow velocity recordings at rest heart rate and at 100 and 120 bpm.
Figure 5. The left atrial circumflex branch (LACB) and left circumflex (LCx) maximal hyperemia coronary flow velocity recordings at rest heart rate and at 100 and 120 bpm.

Figure 6. The left atrial circumflex branch (LACB) baseline coronary flow velocity and pulmonary capillary wedge pressure (mean 5 mm Hg) recordings at rest heart rate.
Study limitations. In the present study, CBF responses were assessed using intracoronary Doppler measurement of CBF velocity. Although the technique by itself is not capable of measuring absolute MP, extensive animal studies have proved the accuracy of Doppler measurements in the assessment of changes in CBF (13,14).

An important limitation of this technique for measuring CBF velocity is the potential for motion artifacts. Nevertheless, because patients with a small LACB and patients with poor-quality recordings were excluded, the data we present in this study represent a fairly accurate assessment of atrial MP.

Although LV end-diastolic pressure was 7 ± 3 mm Hg before and 10 ± 4 mm Hg after the volume load of angiography, diastolic abnormalities of the LV and subtle coronary artery disease may have existed in some of these patients, and our findings may not represent findings in an entirely normal population. Further investigations in different groups of patients are needed to define the physiology and pathophysiology of atrial MP.

Clinical implications. Although not applicable to all patients in the catheterization laboratory, the use of the intracoronary Doppler guide wire in arteries that supply the atria is a novel technique that could provide useful data on atrial MP in atrial pathology.

In the case of an intermediate-severity proximal LCx stenosis, early exhaustion of CFR in the LACB could lead to inadequate atrial MP, despite acceptable CFR in the LCx. If these findings are confirmed in the setting of obstructive coronary artery disease, the currently used cutoff value for CFR in assessing the physiologic significance of intermediate-severity lesions (15,16) may need to be re-evaluated for proximal LCx lesions, to avoid the consequences of left atrial ischemia (17).

Conclusions. The findings of this study show that the CBF of the left atrium is out of phase with that of the ventricular myocardium, showing a predominant systolic pattern.

Although atrial and ventricular CFR show no statistically significant differences at rest and at two levels of stress, the disproportionate increase in atrial compared with ventricular CBF velocity during stress indicates a peculiarity of atrial MP regulation, leading to early exhaustion of vasodilator reserve.

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REFERENCES