In Vitro Investigation of the Impact of Aortic Valve Stenosis Severity on Left Coronary Artery Flow

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2 Methods

2.1 Experimental Model. For the purpose of this study, we modified our validated ventriculo-aortic model [14] by the addition of an in vitro coronary model based on the theoretical model described by Judd and Mates [15]. The hydraulic analog is shown in Fig. 1. The coronary flow model was made up of a soft tube connected to the left coronary ostium of the aorta, which comprises a flow probe, a valve resistance \( R_v \) mimicking the arteriolar resistance, and a bifurcation including a valve resistance \( R_w \) on one hand, and a systolic resistor simulating intramyocardial stresses \( \text{Sim} \) on the other hand, depending on the LV pressure. The systolic resistor was based on the model used by Sabbah and Stein [11]. The pressure surrounding the collapsible tube of the systolic resistor was transmitted from the LV and adjusted by using a valve resistance \( R_v \). This collapsible tube was made of silicone and contributed in part to the compliance in our in vitro coronary model. The outlet of the coronary flow model was connected to the main reservoir of the in vitro aortic flow model.

2.2 Aortic Stenosis Model. To simulate AS, we designed and built a locking system to block the opening of the leaflets of a bioprosthetic aortic valve. A series of screws was inserted in the aortic wall around a 27 mm aortic Mitroflow SynergyTM PC valve and covered with a piece of elastic tube in order to protect the valve (see Fig. 2(a)). The screws were used to control the opening displacement of the valve leaflets (Fig. 2). This system allowed us to vary AS severity from 0% \( \text{EOA}=2.8 \text{ cm}^2 \) to a maximum of about 90% \( \text{EOA}=0.28 \text{ cm}^2 \) (this means that the valve EOA was reduced, for example, by 90%). In this paper, four different AS severities were studied as presented in Table 1: 0% mimicking a normal aortic valve \( \text{EOA}=2.8 \text{ cm}^2 \), 25% mimicking a moderate AS \( \text{EOA}=1.4 \text{ cm}^2 \), 50% mimicking a severe AS \( \text{EOA}=0.7 \text{ cm}^2 \), and 90% mimicking a very severe AS \( \text{EOA}=0.28 \text{ cm}^2 \).

2.3 Experimental Conditions. A Millar catheter (SPC 360S, accuracy of 0.5% full scale) was introduced downstream of the aortic valve in order to measure the aortic pressure. A second Millar catheter was directly introduced in the LV outflow track to measure the instantaneous LV pressure. The aortic flow and left coronary inflow were measured using two electromagnetic flowmeters (Carolina Medical Electronics, East Bend, NC, 600 series, internal diameter=20 mm and 4 mm, respectively, accuracy of 1% full scale). All measurements were performed simultaneously under a wide range of physiologic and pathologic conditions. The aortic flow model was first adjusted to obtain typical normal hemodynamic conditions (Stroke volume=70 ml, systolic blood pressure=120 mm Hg, and diastolic blood pressure=80 mm Hg) at 70 bpm. Then, the resistance and compliance of the coronary section were adjusted in a manner that the coronary flow waveform and its mean value were similar to the ones observed in normal subjects (without AS).

3 Results

As shown in Fig. 3, simulated aortic and LV pressures and aortic flow rate in normal conditions (without AS) were comparable to that observed in human beings [13]. In addition, the amplitude and shape of the coronary flow rate in our in vitro model without AS were similar to in vivo measurements obtained in a normal subject under physiological conditions, as described by Hozumi et al. [16]. In early systole, in this subject, a fast flow rate drop toward zero flow appeared due to the compression of the subendocardial coronary vessels (via a high intraventricular pressure). Over the rest of systole, the heart muscles were still contracted and very little flow occurred in the coronary artery. During diastole, the heart muscles were relaxed, the lumen of the intramyocardial arteries was fully opened, and the major portion of the coronary flow occurred.

In addition, the flow conditions (LV pressure and coronary flow rate) in the in vitro model with an AS (Fig. 4) were in agreement with those reported in patients [8,9]. As can be observed in Fig. 4 and in Table 1, the presence of an AS induced significant increases in the mean coronary flow rate (approximately 73% for a very severe AS), the maximum coronary flow rate (approximately 97% for a very severe AS), and the maximum LV pressure (approximately 88% for a very severe AS). Similarly, variations in EOA were inversely proportional to the variations in the mean coronary flow rate, maximum coronary flow rate, and maximum LV pressure. Furthermore, there was a huge increase in the coronary flow.

Table 1 AS severity in relation to aortic valve EOA. Values of the coronary flow rate \( Q_c \) and the left ventricular pressure \( LVP \) for the four different values of EOA. The variations are calculated in relation to the value obtained in the case without aortic stenosis \( \text{EOA}=2.8 \text{ cm}^2 \). % systolic \( Q_c \) means the percentage of mean systolic coronary flow rate in relation to the total mean coronary flow rate.

<table>
<thead>
<tr>
<th>EOA ((\text{cm}^2))</th>
<th>2.8</th>
<th>1.4</th>
<th>0.7</th>
<th>0.28</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS severity (%)</td>
<td>0</td>
<td>50</td>
<td>75</td>
<td>90</td>
</tr>
<tr>
<td>Qc max (mL/min)</td>
<td>108.9</td>
<td>115.3</td>
<td>134.8</td>
<td>214.2</td>
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<tr>
<td>Variations (%)</td>
<td>0</td>
<td>6</td>
<td>24</td>
<td>97</td>
</tr>
<tr>
<td>Qc mean (mL/min)</td>
<td>56.9</td>
<td>61.4</td>
<td>61.5</td>
<td>98.2</td>
</tr>
<tr>
<td>Variations (%)</td>
<td>7</td>
<td>8</td>
<td>8</td>
<td>73</td>
</tr>
<tr>
<td>% systolic Qc</td>
<td>33.9</td>
<td>30.4</td>
<td>28</td>
<td>24.6</td>
</tr>
<tr>
<td>LVP max (mm Hg)</td>
<td>118.9</td>
<td>132.2</td>
<td>165.3</td>
<td>223.5</td>
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<tr>
<td>Variations (%)</td>
<td>0</td>
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<td>39</td>
<td>88</td>
</tr>
<tr>
<td>LVP mean (mm Hg)</td>
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<td>37.5</td>
<td>50.9</td>
<td>71.1</td>
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<tr>
<td>Variations (%)</td>
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<td>40</td>
<td>95</td>
</tr>
<tr>
<td>Reverse flow (Yes/No)</td>
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<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Qc min (mL/min)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-41.6</td>
</tr>
</tbody>
</table>

Fig. 1 Schema of the in vitro flow model

Fig. 2 Schema of the locking system of the aortic valve leaflets
rate at the beginning of diastole. The majority of this mean coronary flow rate increase occurred during diastole (about 80% throughout diastole and 20% throughout systole). Moreover, when the AS is very severe, at the beginning of systole, the coronary flow rate became retrograde (with a minimum flow rate around $-41 \text{ mL/min}$), as reported in previous studies [8,17,18], while it remained anterograde without AS and for other AS severities (with a minimum flow rate of about 0 mL/min in all cases). The suction produced by the so-called “Venturi effect” of the aortic flow jet was suggested to be responsible for this reverse in flow [17,19]. However, several investigators have questioned the validity of this mechanism [11,20], some arguing that the flow is not reversed in the right coronary artery [20,21]. But the fact that the compression level is not the same between the left and right sides of the heart due to the pressure difference between the two ventricles could explain that the suction is less important in the right coronary artery. In vivo, it has been shown that the presence of an AS induces an increase in the ventricular activity due to a greater demand in myocardial oxygen consumption [1]. Consequently, the mean coronary flow rate increased (via a decrease in the coronary pressure), which allowed an additional contribution of oxygen and energy to the myocardial muscles. In the presence of an AS, the percentage of the mean systolic coronary flow rate decreased with increasing AS severity, due to the marked increase in LV pressure during systole (Table 1).

4 Conclusions

This study allowed us to validate our coronary in vitro model under physiological conditions, both in the absence and presence of AS. We have shown that AS induced important modifications on the normal left coronary artery flow. The two main changes were an increase in the maximum and mean coronary flow rates, and the occurrence of a retrograde flow during systole for a very severe AS. These changes could explain the fact that even if patients have angiographically normal epicardial coronary arteries, we can observe the occurrence of angina pectoris in these patients in the presence of an AS [1].

References


[16] Hozumi, T., Yoshida, K., Ogata, Y., Akasaka, T., Asami, Y., Yagi, T., and


