Cardiac Performance After Diagnostic Coronary Arteriography


SUMMARY
Cardiac performance was assessed before and after diagnostic coronary arteriography in 19 patients with heart disease. There was no significant change in cardiac output, heart rate, stroke volume, hemoglobin, hematocrit, and mean systemic arterial pressure. Left ventricular (LV) filling pressure and mean pulmonary artery pressure increased temporarily. The increased left ventricular filling pressure was accompanied by an increase of LV work performed in a few patients; in the remainder the left ventricle performed less work.

In four dogs, selective left coronary arteriography resulting in increased ventricular filling pressure, was accompanied by an increase of left ventricular end-diastolic (VED) and stroke volumes; the ejection fraction and heart rate remained unchanged.

If the animal studies (increased VED accompanying increased ventricular filling pressure) can be applied to patients with heart disease, the alteration of left ventricular function can be considered on the basis of the Frank-Starling mechanism. To cope with the temporary depression of its function, the left ventricle of patients with heart disease utilized the Frank-Starling mechanism resulting in an adequate (essentially unchanged) cardiac output from an increased left ventricular filling pressure. The normal left ventricle of the dog, stressed more than is appropriate clinically, shows an increased stroke volume accompanying the increased end-diastolic volume.

Additional Indexing Words:
Frank-Starling mechanism Coronary artery disease Contrast medium
Ventricular volume Ventricular pressure

RAPID INJECTION of large amounts (1.0 to 1.8 ml/kg) of contrast medium into the circulation for diagnostic angiography has been shown to cause transient increase in cardiac output (18 to 94%), plasma osmolality (9%), and circulating blood volume (10%). These changes in the circulation cause an increase of pressure gradients across stenotic valves and an alteration in ventricular performance. Patients with a normal left ventricle consistently respond by an increase of pressure-volume work performed and patients who have heart disease respond either normally, that is, by an increase in the work performed, or abnormally, that is, with no change or a decrease in the work performed.

Selective coronary arteriography differs from diagnostic angiography. It involves repeated (five to eight or more) injections of small amounts (4 to 8 ml) of contrast medium directly into the coronary arteries, over a period of time. This study describes cardiac performance following diagnostic coronary arteriography in patients with

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heart disease. It demonstrates temporary depression of left ventricular function and suggests that the left ventricle utilizes the Frank-Starling mechanism to maintain adequate circulation.

Methods

Clinical Studies

Nineteen patients (15 males, four females), all with heart disease, aged 34 to 59 years (mean, 51.5 years), were studied. Twelve patients had coronary artery disease (CAD), three had CAD with valvular heart disease, one had CAD with an atrial septal defect, one had subvalvar mitral incompetence, and two had congestive cardiomyopathy. The diagnosis of coronary artery disease was established by selective coronary arteriography. During the study there were no complications, no episodes of ischemic cardiac pain, and no dysrhythmias in any of the 19 patients, apart from bradycardia of a few seconds' duration in some of the patients.

Cardiac catheterization and selective coronary arteriography were carried out for diagnostic purposes. Pressures in the left ventricle, ascending aorta, and the right side of the heart were recorded via cardiac catheters; systemic arterial pressures were recorded via a 6-inch piece of red Kifa tubing. Statham strain gauges (P23Gb series) were used, and all the variables were recorded on photographic paper using an Electronics for Medicine recorder (model DR 8). Mean atrial and arterial pressures were obtained by electrical damping.

Cardiac output (CO) was determined by the indicator-dilution technic according to the method of Hamilton and associates. Indocyanine green was injected into the pulmonary artery; the sampling sites were the femoral or brachial artery. Blood was withdrawn at a rate of 35 to 45 ml/min past a Gilford densitometer (model 103iR) and the change in optical density associated with the passage of dye was amplified and recorded on a Honeywell strip-chart recorder. Heart rate was obtained from the electrocardiogram. Blood hemoglobin and packed cell volume (PCV) were determined in the standard manner.

The left ventricular stroke work (LVSW) was computed as follows: LVSW (g-m) = (LVSP - LVEDP) \times SV \times 0.0144 where LVSP is the mean left ventricular systolic pressure obtained by planimetric integration, LVEDP is the left ventricular end-diastolic pressure, SV is the stroke volume obtained from the cardiac output and heart rate, and the factor 0.0144 allows the result to be expressed in conventional units (gram-meters).

Selective coronary arteriography was performed using Hypaque 65%.* Hypaque 65% has the following characteristics: 25% w/v sodium and 50% w/v N-methylglucamine diatrizoate, iodine content, 39 g/100 ml, pH 7.4, viscosity at 37 C 6.45 centipoises, osmolality greater than 1,600 mOsm/L (determined in our laboratory), specific gravity 1.426, and sodium content, 9 g or 391 mEq/L.

Procedure

Prior to cardiac catheterization the patients were medicated with a mixture of meperidine and promethazine (Demerol and Phenergan). Right and left heart pressures were recorded and blood withdrawn for hemoglobin and PCV determination. Two indicator-dilution curves were recorded in rapid succession; the mean CO calculated from these two curves was used as the control value. Selective coronary arteriography was performed by the technic of Sones and Shirey or Judkins using Hypaque 65%. Five to eight milliliters of Hypaque 65% was injected five to eight times into each patient within 10 to 30 minutes. Right and left heart pressures were again recorded; blood was withdrawn for hemoglobin and PCV determinations, and two indicator-dilution curves were obtained. The determinations made after coronary arteriography were completed within 5 to 10 minutes after all the arteriograms had been obtained. Almost all the patients then had a left ventricular cineangiogram taken, but by this time all the determinations for this study had been made. All the parameters were not determined in each patient.

Experimental Studies

Four mongrel dogs were anesthetized with intravenous pentothal, and further anesthesia was maintained with intermittent intravenous administration of pentobarbital (Nembutal). The left atrium (LA) was catheterized by introducing a Muller catheter from the right carotid artery retrogradely into LA via the aortic and mitral valves. The left ventricle was catheterized by introducing a no. 9 NIH catheter from the left carotid artery. The left coronary artery was intubated by introducing a Judkins coronary artery catheter from the right femoral artery. Left atrial and left ventricular pressures were recorded with strain gauges (Statham P23Db), on photographic paper using an Electronics for Medicine recorder (model DR 8).

Once the catheters were in position, the animals were placed in the right antero-oblique position and fluoroscopic and cineangiographic

apparatus were placed into position. The animal and apparatus were not moved until the end of the experiment.

Left atrial (LA) and left ventricular (LV) pressures were recorded, and one-plane left ventricular cineangiogram was made at 48 frames/sec. For the cineangiogram, 20 ml of 76% Urografin* was injected rapidly by hand into the left ventricular cavity. Fifteen to twenty minutes later, at least 10 minutes after the LVEDP and LA pressures had returned to normal, 2 to 4 ml of Hypaque 65% was repeatedly injected into the left coronary artery until a substantial elevation of LVEDP and LA pressures was obtained. LV and LA pressures were recorded, and LV cineangiography was performed. Fifteen to twenty minutes later, at least 10 minutes after the pressures had returned to the control value, the LV and LA pressures were recorded, and LV cineangiography was repeated. Once the catheters were in position, the rest of the procedure took about 40 to 50 minutes.

Left ventricular volumes were calculated from one-plane cineangiograms according to Greene and associates' modification of the method of Gribbe and associates. This modification assumes that the third (unvisualized) axis, depth from septum to free wall, is of the same magnitude and behaves in the same way as the visualized short axis. Greene and co-workers found the third axis to average 7% less than the assumed value of the third axis in man, while Gribbe and associates found in dogs that the third axis averaged 15% (± 5.3% SD) less than the assumed value of the third axis. In any one animal we were looking basically for changes in volume during the different states; therefore, the animal and x-ray equipment were not moved after being placed in position, and in the final calculations no correction was made for the magnification of the ventricular dimensions by x-rays. To check that the magnification factor was unchanged, the catheter diameter was measured in the frames prior to each LV cineangiogram and was found to be identical for the three states in each animal. The catheter diameter on the x-ray frame averaged an increase of less than 5% as compared with the catheter diameter outside the body. Thus the values of ventricular volumes calculated will be a little in excess of the actual ventricular volumes.

Results

The mean difference, standard error of the mean, and P value for the paired values before and after coronary arteriographic determinations are shown in table 1. Also shown in the same table are the average and the range of the percentage changes in the various parameters following coronary arteriography. There was no significant change in cardiac output, heart rate, stroke volume, hemoglobin, packed cell volume, and mean aortic pressure (P values ranging from 0.1 to 1.0). There was a significant increase in LVEDP, mean PA wedge pressure, mean PA pressure, RVEDP, and mean RA pressure, the

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*Urografin, Schering AG, Berlin, Germany.

**Table 1**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients no.</th>
<th>Paired differences</th>
<th>Per cent change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SEM</td>
<td>P</td>
</tr>
<tr>
<td>Cardiac output (L/min)</td>
<td>11</td>
<td>0.073</td>
<td>0.125</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>18</td>
<td>1.333</td>
<td>1.446</td>
</tr>
<tr>
<td>Stroke volume (ml/min)</td>
<td>11</td>
<td>4.700</td>
<td>2.144</td>
</tr>
<tr>
<td>Hemoglobin (g/100 ml)</td>
<td>9</td>
<td>−0.389</td>
<td>0.209</td>
</tr>
<tr>
<td>Packed cell volume</td>
<td>9</td>
<td>−1.667</td>
<td>1.067</td>
</tr>
<tr>
<td>Aortic or systemic arterial pressure (mm Hg)</td>
<td>14</td>
<td>0.000</td>
<td>2.191</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>12</td>
<td>5.833</td>
<td>1.290</td>
</tr>
<tr>
<td>Mean PA wedge pressure (mm Hg)</td>
<td>17</td>
<td>4.471</td>
<td>0.733</td>
</tr>
<tr>
<td>Mean PA pressure (mm Hg)</td>
<td>17</td>
<td>4.118</td>
<td>0.984</td>
</tr>
<tr>
<td>RVEDP (mm Hg)</td>
<td>17</td>
<td>1.647</td>
<td>0.383</td>
</tr>
<tr>
<td>Mean RA pressure (mm Hg)</td>
<td>17</td>
<td>1.588</td>
<td>0.364</td>
</tr>
</tbody>
</table>

Abbreviations: PA = pulmonary artery; RA = right atrium; LVEDP and RVEDP = left and right ventricular end-diastolic pressures, respectively; SEM = standard error of the mean.

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mean increases being 5.8, 4.5, 4.1, 1.6, and 1.6 mm Hg respectively, and the *P* values ranging from 0.0005 to 0.000009. The percentage increases in LVEDP (51%) and mean PA wedge pressure (35%) are different as the LVEDP was available in only 12 patients. The range of increase in left ventricular filling pressure was 7 to 114%. The percentage change in right ventricular filling pressures was 24% with a range of 0 to 66%. The increase in mean PA pressure was probably the result of increase of left ventricular filling pressures. Changes in right ventricular filling pressure were small: no change in six, 1 to 2 mm Hg elevation in six, and 3 to 4 mm Hg elevation in four.

The left ventricular filling pressures, LVEDP or mean PA wedge pressure, before and after coronary arteriography in all 19 patients are given in figure 1. The LV filling pressures increased in all; in some the increases were small (few mm Hg); in others the increases were large (8 to 13 mm Hg). There was no consistent relation between the clinical status of the patient and the increase in the LVEDP. The patient with an initial LVEDP of 30 had congestive cardiomyopathy and an increase of 2 mm Hg.

In figure 2 are depicted plots of selected values of mean PA wedge pressure from a continuous record in two patients. The prearteriographic value, that is, the control value, was normal in one patient at 10 mm Hg and abnormal in another at 20 mm Hg. With selective injection of contrast medium into the coronary arteries (indicated by arrows) a more or less progressive increase of the mean PA wedge pressure occurred in both patients. For each determination of mean PA wedge pressure, the patient was returned to the supine position in order that the zero reference level would remain unchanged.

Figure 3 shows the relation of LVSW to LVEDP before and after coronary arteriography.
CORONARY ARTERIOGRAPHY

phy in nine patients in whom LVSW could be computed. The increased LVEDP after coronary arteriography was accompanied by an increase of LVSW in three patients (in one only minimally) and a decrease of LVSW in the remaining six.

As the mean aortic pressure and heart rate were unchanged, the observed changes in left ventricular function could be considered on the basis of the Frank-Starling mechanism, provided the increased LVEDP was accompanied by an increase in myocardial fiber length or ventricular end-diastolic volume.

To assess possible changes in ventricular volume, four dogs were investigated by selective left coronary arteriography until ventricular filling pressure was elevated. The results in one dog (dog 2, table 2) are shown in detail in figure 4. As the LVEDP increased from 3 to 8 mm Hg, the end-diastolic volume increased from about 82 (left panel) to about 110 (center panel). This increase in end-diastolic volume was accompanied by an increase of the left ventricular stroke volume (V_{ED} - V_{ED}); the ejection fraction (V_{ED} - V_{ED}/V_{ED}) remaining essentially unchanged. During this period the heart rate and left ventricular systolic pressure (not shown in figure) showed no significant change. In the recovery period (panel on the right), all the values had returned to the control level showing that the values in the experimental period were not due to the effects of contrast medium used for the LV cineangiogram in the control period and that our preparation was a viable one. The results in the other three dogs were similar (table 2).

Discussion

Diagnostic coronary arteriography in patients with heart disease consistently resulted in an increase of left ventricular end-diastolic pressure (LVEDP) and mean pulmonary artery wedge pressure. There was a small increase in mean pulmonary artery pressure, probably a result of the increase in LVEDP and there was also a small or no increase in right ventricular filling pressure. The increase of LVEDP was accompanied by an increase of left ventricular stroke work (LVSW) in a few patients and, in the remainder, LVSW decreased. Clearly, left ventricular function is altered by diagnostic coronary arteriography.

Cardiac performance is a complex function and can be altered by changes in end-diastolic volume (pre-load), impedance to ventricular ejection (after-load), inotropic state of the muscle, and frequency of contraction (rate). Heart rate and systemic arterial pressure showed no significant change in the present study and cannot be held responsible for the alteration in cardiac performance. If the result of our experimental studies can be applied to patients with heart disease, then the increase in LVEDP would be expected to be accompanied by an increase in ventricular end-diastolic volume (V_{ED}) and, therefore, the changes in ventricular performance can be considered on the basis of the Frank Starling\textsuperscript{7,8} mechanism.

The blood hemoglobin and hematocrit showed no significant change. Thus, the increase in LVEDP is not due to an increased
Composite left ventricular volume curve end-diastolic pressure, stroke volume, ejection fraction, and heart rate in a dog, weighing 21.4 kg. Each left ventricular volume curve is a composite of 2 to 4 cardiac cycles. In the left panel are the values during the control period, in the center panel those obtained immediately after coronary angiography, and on the right are the values in the recovery period.

Table 2

<table>
<thead>
<tr>
<th>Animal no. and weight</th>
<th>VED</th>
<th>VES</th>
<th>VED - VES (LVSV)</th>
<th>VED - VES/VED (EF)</th>
<th>LVEDP</th>
<th>Heart rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog 1 11.4 kg Control</td>
<td>62</td>
<td>20</td>
<td>42</td>
<td>0.68</td>
<td>2</td>
<td>158</td>
</tr>
<tr>
<td>Dog 1 11.4 kg Experiment</td>
<td>72</td>
<td>36</td>
<td>36</td>
<td>0.50</td>
<td>23</td>
<td>143</td>
</tr>
<tr>
<td>Dog 1 11.4 kg Recovery</td>
<td>56</td>
<td>14</td>
<td>42</td>
<td>0.75</td>
<td>1</td>
<td>150</td>
</tr>
<tr>
<td>Dog 2 21.4 kg Control</td>
<td>82</td>
<td>20</td>
<td>62</td>
<td>0.76</td>
<td>3</td>
<td>207</td>
</tr>
<tr>
<td>Dog 2 21.4 kg Experiment</td>
<td>110</td>
<td>33</td>
<td>77</td>
<td>0.70</td>
<td>8</td>
<td>194</td>
</tr>
<tr>
<td>Dog 2 21.4 kg Recovery</td>
<td>82</td>
<td>20</td>
<td>62</td>
<td>0.76</td>
<td>3</td>
<td>200</td>
</tr>
<tr>
<td>Dog 3 10.5 kg Control</td>
<td>55</td>
<td>29</td>
<td>26</td>
<td>0.47</td>
<td>2</td>
<td>162</td>
</tr>
<tr>
<td>Dog 3 10.5 kg Experiment</td>
<td>70</td>
<td>46</td>
<td>46</td>
<td>0.66</td>
<td>18</td>
<td>158</td>
</tr>
<tr>
<td>Dog 3 10.5 kg Recovery</td>
<td>42</td>
<td>17</td>
<td>25</td>
<td>0.60</td>
<td>3</td>
<td>150</td>
</tr>
<tr>
<td>Dog 4 11.4 kg Control</td>
<td>67</td>
<td>24</td>
<td>43</td>
<td>0.64</td>
<td>5</td>
<td>111</td>
</tr>
<tr>
<td>Dog 4 11.4 kg Experiment</td>
<td>102</td>
<td>43</td>
<td>59</td>
<td>0.58</td>
<td>20</td>
<td>105</td>
</tr>
<tr>
<td>Dog 4 11.4 kg Recovery</td>
<td>74</td>
<td>22</td>
<td>52</td>
<td>0.70</td>
<td>4</td>
<td>118</td>
</tr>
</tbody>
</table>

Abbreviations: VED = end-diastolic volume; VES = end-systolic volume; LVSV = left ventricular stroke volume; EF = ejection fraction; LVEDP = left ventricular end-diastolic pressure.

circulating blood volume known to occur after diagnostic angiocardiology.\textsuperscript{1,3} Contrast medium has been shown to have potent direct negative inotropic effects resulting in reduction of contractility both in normal and failing hearts.\textsuperscript{17} Furthermore, in the intact animal, reduction of the myocardial contractile force has been demonstrated.\textsuperscript{18} Ventricular function was depressed in the patients with heart disease as the left ventricular end-diastolic
volume increased without associated increase of after-load or circulating blood volume and, in many of the patients the work performed by the left ventricle decreased. Depression of ventricular function followed introduction of contrast medium directly into the coronary arteries. The LV utilized a fundamental type of adjustment available to it, namely the Frank-Starling mechanism; LVEDP increased, and an adequate (essentially unchanged) cardiac output was maintained. The normal LV of the dog behaves differently as the increased V ED was accompanied by an increased stroke volume.

The mechanism by which depression of ventricular function occurs following diagnostic coronary arteriography is probably complex, involving many factors. Presence of heart disease is important, as in our studies with the normal left ventricle of the dog many more injections of contrast medium were necessary to elevate the LVEDP than were necessary in patients with heart disease. Repeated injections probably have an additive effect as the LVEDP may not rise with the first injection (fig. 2), and a single injection of contrast medium into the coronary artery has been shown to produce only brief changes lasting up to 1 or 2 minutes. A depressor reflex, initiated by excitation of mechano-receptors arising from the left coronary artery has been described in the cat. If such a reflex is present in man, it would not account for all the observed changes as minimal or no changes are seen when substances other than contrast medium (for example, blood, glucose) are injected into the coronary arteries. Similarly, lack of oxygen in contrast medium appears to be clinically significant when the contrast medium is not washed away rapidly by coronary blood flow. Though changes induced by the high osmolality of the contrast medium may be of significance, it would appear that the high sodium (Na) content of contrast medium is a very important factor in production of the observed changes. The effect seen may be the result of changes at the cellular level from shifts in water and electrolytes, or from an antagonism between calcium and an excess of extracellular sodium or both.

The alteration in cardiac performance in patients with heart disease is temporary, lasting 15 to 60 minutes in a few patients we have studied. For this reason any studies of cardiac performance being assessed at the time of diagnostic coronary arteriography should preferably be completed prior to performing the coronary arteriograms. There appears to be a delay of approximately 6 beats (fig. 5) from the time contrast medium is injected to changes being seen in left ventricular filling pressure and on the electrocardiogram.

Figure 5
A continuous record of the electrocardiogram (ECG) and mean left atrial (LA) pressure in one dog during selective coronary arteriography. With each injection of contrast medium (indicated by arrows) there is a delay of approximately 6 beats before temporary changes are seen in the LA pressure and on the ECG.
Acknowledgment

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