Role of Afterload in Determining Regional Right Ventricular Performance during Coronary Underperfusion in Dogs

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SUMMARY. The relationship between coronary perfusion pressure and regional myocardial performance of the right ventricular free wall was studied, in the presence or absence of right ventricular hypertension in 13 open-chest dogs. The right coronary artery was perfused through a shunt from a carotid artery. Regional systolic shortening of the right ventricular free wall was measured by means of a sonomicrometric technique at various levels of coronary perfusion pressure. Regional shortening was insensitive to coronary perfusion pressure or flow when it was above 31 mm Hg or 0.27 ml/min per g. Once coronary perfusion was below this critical level, regional shortening in both base to apex and circumferential orientations decreased linearly, depending on the degree of perfusion pressure. Despite the presence of a monoexponential relationship between coronary perfusion pressure or flow and regional shortening, a direct linear relation between perfusion pressure and flow was consistently noted, with or without pulmonary artery banding, suggesting that there is limited autoregulation of right coronary flow. The critical perfusion pressure for maintaining regional myocardial function of the right ventricle was highly dependent on the level of right ventricular systolic pressure (r = 0.64 - 0.72, P < 0.05). Thus, right ventricular systolic pressure was one of the important determinants of regional wall motion during coronary underperfusion. (Circ Res 57: 96-104, 1985)

IN the left ventricle, severe coronary arterial stenosis reduces both coronary perfusion pressure and regional myocardial blood flow (Nakamura et al., 1973; Tomoike et al., 1977). This produces regional wall motion abnormalities (Wyatt et al., 1975; Nakamura et al., 1977; Koyanagi, 1979) and subsequent reductions in cardiac output if the ischemic zone is large enough (Lekven et al., 1973; Isoyama et al., 1983). The concept of critical flow below which regional contractile performance deteriorates in proportion to the reduction in perfusion has been documented repeatedly (Wyatt et al., 1975; Downey, 1976; Banka et al., 1977; Vatner, 1980; Weintraub et al., 1981). The critical level of perfusion pressure for maintaining normal regional wall motion in the left ventricle was about 40 to 60 mm Hg (Wyatt et al., 1975; Waters et al., 1977; Banka et al., 1977; Koyanagi, 1979). However, the relationship between coronary perfusion pressure and regional wall motion in the right ventricle remains poorly understood.

Accordingly, in the present study, we examined the effects of graded reductions in regional coronary perfusion pressure on regional segment shortening in the right ventricular free wall. Because afterload influences the extent of regional wall motion during systole (Lekven and Kiil, 1975; Sasayama et al., 1980), segment shortening was measured with and without an increased level of right ventricular pressure induced by constricting the pulmonary artery.

Methods

Thirteen mongrel dogs (19-23 kg) were sedated with intramuscular morphine sulfate (10 mg) and then anesthetized with the intravenous α-chloralose (45 mg/kg) and urethane (450 mg/kg). After endotracheal intubation, a left thoracotomy at the 3rd intercostal space was performed under positive pressure respiration and the pericardium was opened. A hydraulic vascular occluder (φ = 16 mm) was placed around the main pulmonary artery. The pericardium was loosely closed, and the chest was closed. A right thoracotomy then was performed through the 4th intercostal space, and the heart was supported in a pericardial cradle. The autoperfusion system from the right carotid artery to the proximal portion of the right coronary artery was established using a large bore cannula (Fig. 1). Right coronary blood flow and pressure were monitored by a cannulating type electromagnetic flow probe (φ = 3 mm, Statham, SP7517) and Statham P23Db transducer, respectively, as shown in Figure 1. A zero level flow signal was obtained, both in normal saline solution and during coronary occlusion. There was no significant shift in zero level between in vitro and in situ calibration. At the end of the experiment, the flow probe was calibrated with blood, and the correlation coefficient between flow probe measurements and volumetric measurements was above 0.98. Systemic arterial pressure was monitored continuously at the ascending aorta with a P23Db pressure...
Urabe et al. / Afterload and Right Ventricular Function

**Results**

**Hemodynamic Changes before and after Pulmonary Artery Banding (Table 1)**

Heart rate, mean aortic pressure, left ventricular (LV) systolic pressure, LV diastolic pressure, and LV dP/dt were unchanged before and after PA banding (Table 1). Right ventricular (RV) systolic pressure increased from 30 ± 7 mm Hg to 45 ± 9 mm Hg (P < 0.01), and RV diastolic pressure increased slightly, but not significantly, from 2.8 ± 1.5 mm Hg to 3.0 ± 1.8 mm Hg, after PA banding. Mean coronary blood flow increased from 16.3 ± 4.5 ml/min (0.71 ± 0.22 ml/min per g) to 21.1 ± 8.6 ml/min (0.94 ± 0.34 ml/min per g) (P < 0.01) after PA banding. End-diastolic lengths of base to apex and circumferential segments and the areas calculated from these lengths increased significantly after PA banding. The systolic to diastolic flow ratio of the right coronary artery derived from planimetry of the coronary blood flow tracings during systole and diastole.

All data are presented as mean ± se. Statistical analysis of the data was performed by analysis of variance and paired t-test. Linear regression analysis was performed to determine the slope, intercept, and correlation coefficient between the perfusion pressure and coronary blood flow. Monoexponential curve fitting was performed on normalized data of coronary perfusion pressure or blood flow and regional shortening.

**Figure 2** shows representative recordings of regional wall motion and coronary perfusion pressure or perfusion flow.
flow before (upper panel) and after (lower panel) PA banding. Before PA banding, regional wall motion remained almost constant at the perfusion pressure of 48 mm Hg, and then decreased progressively, depending on the level of perfusion pressure (Fig. 2, upper panel). When right ventricular systolic pressure was increased by 25 mm Hg (Fig. 2) without affecting mean arterial and left ventricular peak systolic pressures, regional hypokinesis was first noted at a perfusion pressure of 60 mm Hg. The relationship between right coronary perfusion pressure and regional shortening is plotted in Figure 3. Regional shortening was insensitive to changes in right coronary perfusion pressure when the pressure

Results are expressed as mean ± so. NS = not significant; PA = pulmonary artery; RVSP = right ventricular systolic pressure; RVEDP = right ventricular end-diastolic pressure; RV dp/dt = first derivative of right ventricular pressure; AoP = aortic pressure; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; LV dp/dt = first derivative of left ventricular pressure; CBF RCA = perfusion flow of the right coronary artery; EDL = end-diastolic length; B-A = base-to-apex; CIR = circumferential; PP-flow = perfusion pressure-flow relation; P = probability.

FIGURE 2. Effects of various levels of perfusion pressure on right ventricular pressure and segment length from a representative experiment. The upper panel shows tracings taken at the normal right ventricular pressure as a control, and the lower panel shows tracings taken during pulmonary artery (PA) banding. Perfusion pressure was varied by constricting the by-pass tract from the right carotid artery to the right coronary artery, as shown in Figure 1. After abrupt changes in coronary perfusion pressure, coronary blood flow changed, depending on the pressure level, and was always maintained constant during the procedure; thus this phenomenon indicates the absence of autoregulation in the right coronary vasculature. Right ventricular pressure was increased by constricting the pulmonary artery with a cuff occluder. Note that an exaggerated regional dysfunction during right ventricular hypertension was obvious, even at the comparative coronary perfusion pressure. A reactive hyperemia was always noted and the degree of the reactive hyperemia depended on the reduced level of coronary perfusion pressure. RCA = right coronary artery; PP = perfusion pressure (in mm Hg); RV = right ventricle.
Figure 3. Right coronary artery (RCA) perfusion pressure-regional shortening (%) data from a representative dog before (closed circle) and after (open circle) PA banding. Left and right panels show data obtained at the base-to-apex and circumferential planes, respectively. Curve falls off steeply below the perfusion pressure at the inflection point (indicated by an arrow), showing the presence of critical perfusion pressure unique to the regional right ventricular free wall, after which regional wall motion became highly dependent on the perfusion pressure. PA banding obviously shifts this relation toward the right.

exceeded a "critical" level. Below this perfusion pressure, the regional shortening of base to apex and circumferential segments were directly dependent on right coronary perfusion pressure. In Figure 4, all data points in each dog are replotted to demonstrate the pressure-shortening relation (Fig. 4A) and flow-shortening relation (Fig. 4B) in the right ventricle. The inflection points, below which the regional shortening was dependent on perfusion pressure, were estimated by visual inspection (arrows in Fig. 3). The average inflection pressure was 30 ± 9 (SD) and 45 ± 16 mm Hg before and after PA banding, respectively, (P < 0.01) in the base-to-apex segment and 32 ± 6 and 42 ± 11 mm Hg before and after PA banding, respectively, (P < 0.01) in the circumferential segment (Table 2). There was no significant difference in the level of critical perfusion pressures between the base-to-apex and the circumferential segments.

A monoeponential curvilinear relation between perfusion pressure or flow rate and percent shortening was noted before and after PA banding. It is noteworthy that the relationship is shifted rightward after PA banding (Fig. 3). In Figure 5, the relationship between coronary perfusion pressure or flow and systolic shortening in the circumferential direction is replotted by normalizing the perfusion pressure, flow, and regional shortening data as decimal fractions of the data observed at the inflection point. A highly significant correlation coefficient was obtained when normalized pressure (X) and shortening (y) were fitted to a monoeponential curve after transforming the ordinate into y’ = y + 1.5. The equations derived for data from all 13 open-chest dogs were: y’ = 70X^0.24 (r = 0.67, n = 126, P < 0.001) in the base-to-apex direction at normal RV pressure, y’ = 25X^0.44 (r = 0.72, n = 118, P < 0.001)
Relationship between Shift in Critical Perfusion Pressure and RV Systolic Pressure

Increases in RV systolic pressure during PA banding were directly related to the level of critical perfusion pressure, as shown in Figure 6. Correlation coefficients and slopes between changes in systolic RV pressure and critical perfusion pressure were practically the same between the base-to-apex and the circumferential planes (Fig. 6).

### Table 3

<table>
<thead>
<tr>
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<th>Perfusion pressure</th>
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<tr>
<td></td>
<td>Above critical pressure</td>
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<tr>
<td></td>
<td>RV† Normotension Hypertension</td>
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<tr>
<td>LVSP (mm Hg)</td>
<td>-0.9 ± 3.4 -0.3 ± 2.0</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>-0.1 ± 0.7 -0.1 ± 0.3</td>
</tr>
<tr>
<td>LV dP/dt (mm Hg/sec)</td>
<td>37 ± 115 -56 ± 144</td>
</tr>
<tr>
<td>RVSP (mm Hg)</td>
<td>-0.1 ± 1.1 -0.4 ± 1.8</td>
</tr>
<tr>
<td>RVEDP (mm Hg)</td>
<td>0.1 ± 0.3 -0.2 ± 0.2</td>
</tr>
<tr>
<td>RV dP/dt (mm Hg/sec)</td>
<td>1 ± 40 -17 ± 30</td>
</tr>
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Results are the difference between variables before and during coronary underperfusion and are expressed as mean ± so. Abbreviations as in Table 1.

* P < 0.05 by paired t-test between results obtained before and during coronary hypoperfusion.
† Right ventricular pressure in either normotensive or hypertensive dogs.
Effects of Coronary Underperfusion on Right and Left Ventricular Pressures

Changes in right and left ventricular pressures during coronary underperfusion are summarized in Table 3. Although statistically significant reductions in right and left ventricular systolic pressures and some increases in right ventricular end-diastolic pressure were noted during pulmonary artery banding below the critical perfusion pressure, these changes were too small to consider as physiologically significant alterations. Thus, a marked reduction of regional function in the right ventricular free wall did not affect global performance of either the right or left ventricle.

Relationship between Coronary Perfusion Pressure and Coronary Blood Flow

In the phasic pattern of right coronary blood flow, systolic dominant flow was consistently noted, and the systolic-to-diastolic flow ratio decreased significantly after the PA banding (Table 1). Coronary perfusion pressure correlated rectilinearly with the level of mean coronary blood flow, as shown in Figure 7. The slope of the rectilinear relation between perfusion pressure and coronary blood flow at the control RV pressure decreased slightly but significantly above (closed circles) the inflection points, but the slope change above the inflection point during RV hypertension was not significant (Table 4). The critical flow level for the base to apex and the circumferential segments was not different (Table 2). Coronary flow at the inflection point increased after pulmonary artery banding from 0.27 ± 0.12 to 0.44 ± 0.19 ml/min per g (P < 0.01) in the base to apex plane and from 0.27 ± 0.08 to 0.39 ± 0.16 ml/min per g (P < 0.01) in the circumferential plane. The systolic to diastolic flow ratio decreased slightly at the critical level of right coronary perfusion; in RV normotension, it decreased from 1.28 ± 0.24 to 1.09 ± 0.16 (P < 0.01) and during RV hypertension it did not change significantly (1.05 ± 0.11 to 1.00 ± 0.16). The slope of the linear relation between the perfusion pressure and coronary flow increased significantly (P < 0.05) from 0.0083 ± 0.0025 to 0.012 ± 0.0040 ml/min per g per mm Hg after RV hypertension induced by pulmonary artery banding.

Discussion

Using an autoperfusion system from the carotid artery to the right coronary artery, we studied the effects of graded reductions in coronary perfusion pressure on regional wall motion in the right ventricular free wall with and without pulmonary artery banding. Independent control of ventricular cavity pressure and perfusion pressure was experimentally
artery banding may be attributable to the elevation level of critical perfusion pressure during pulmonary of right ventricular pressure. An increase of afterload increased degree of the critical perfusion pressure and resulted in a rightward shift of the relationship between perfusion pressure and regional wall motion similar to that of the left ventricle (Wyatt et al., 1975), but the critical perfusion pressure was lower in the right than in the left ventricle. An increase in RV afterload elevated the critical perfusion pressure below which regional function deteriorated, (3) wall motion abnormalities appeared at the same perfusion pressure, irrespective of the direction of segment length measurements, and (4) right coronary blood flow did not autoregulate in the same manner as left coronary blood flow.

Coronary Perfusion Pressure as a Determinant of Regional Myocardial Performance

Several researchers documented a significant relationship between regional myocardial shortening or thickening and mean coronary flow (Wyatt et al., 1975; Forrester et al., 1976), regional myocardial flow (Banka et al., 1977; Vatner, 1980; Gallagher et al., 1980; Weintraub et al., 1981) or perfusion pressure (Wyatt et al., 1975). It was repeatedly observed that below a critical level of perfusion pressure (flow), wall motion deteriorates progressively, depending on the reduction of perfusion pressure (flow). The level of a critical perfusion pressure was 50–60 mm Hg in the left ventricle (Wyatt et al., 1975; Banka et al., 1977; Koyanagi, 1979). However, the critical level of perfusion pressure or flow for maintaining right ventricular function was not previously examined. In the present study, substantial deterioration of regional wall motion was first observed at approximately 25–35 mm Hg of perfusion pressure. Thus, regional right ventricular function is maintained well at a lower level of coronary perfusion pressure than the left ventricle. The difference in the critical perfusion pressure between the right and left ventricles may be explained by (1) a marked difference in afterload for performing systolic wall motion, (2) lower oxygen consumption of the right than the left ventricle due to the lower level of right ventricular pressure and work (Arnold et al., 1968; Henquell and Honig, 1976) and thinner wall thickness of the right than the left ventricle.

Effects of Increased Afterload on the Perfusion Pressure-Regional Shortening Relation

An increase in the right ventricular pressure resulted in a rightward shift of the relationship between perfusion pressure and regional shortening. A direct linear relation was noted between the increased degree of the critical perfusion pressure and that of right ventricular systolic pressure. The higher level of critical perfusion pressure during pulmonary artery banding may be attributable to the elevation of right ventricular pressure. An increase of afterload increases myocardial oxygen consumption, as suggested by an increase of pressure-rate product (Isoyama et al., 1983; Lekven and Kiil, 1975). However, a direct measurement of right ventricular oxygen consumption was not feasible in the present study because it was impossible to sample the venous effluent from the right ventricle due to its Thebesian drainage and the small size of right ventricular veins.

In the present study, RV end-diastolic pressure tended to increase, but not significantly, after PA banding. End-diastolic segment lengths increased significantly after PA banding. In addition, an area of the RV free wall was calculated from end-diastolic lengths of the base-to-apex and circumferential segments to obtain a parameter of preload which is less sensitive to the geometric effect of ventricular chamber configuration (Raines et al., 1976), and this also increased significantly after PA banding. The wall tension calculated from a pressure and area at end-diastole by Laplace's law increased significantly, suggesting an augmentation of preload. Ellis and Klocke (1979) described a rightward shift of the pressure-flow relation of the left coronary artery during diastole when the preload was increased, and suggested that this was accompanied by an increase in intramyocardial pressure. Accordingly, the rightward shift of the pressure-segment shortening relation during PA banding in our study may be explained in part by the increases in preload following RV hypertension.

Wyatt et al. (1977) described that a primary increase in afterload reduced cardiac output but improved regional myocardial wall motion and perfusion. The beneficial effect of an increase in afterload was also demonstrated by restoration of lactate uptake by the ischemic myocardium. The difference of the present results from those of Wyatt et al. (1977) might be derived from the independent alteration of coronary perfusion pressure from the right ventricular cavity pressure during afterload increase in the present model.

Critical Perfusion Pressure and Autoregulation

The slope of the perfusion pressure-coronary flow relation at the normal RV pressure was decreased (P < 0.05 - 0.01) above the critical perfusion pressure, and this phenomenon suggests the partial operation of an autoregulatory mechanism in the vascular bed supplied by the right coronary artery. However, the reduction in the slope of the perfusion pressure-coronary flow relation above the inflection point was eliminated during pulmonary artery banding. Thus, a linear relation between perfusion pressure and flow in the right coronary artery was apparent. This observation is quite different from previous data on the left ventricle (Mosher et al., 1964; Banka et al., 1977), in which a curvilinear relation between pressure and flow was noted and autoregulation was proposed to describe the phenomenon of stable coronary flow, despite changes in coronary perfu-
tion pressure. The apparent absence of autoregulation could be explained by: (1) right coronary vasculature that was maximally dilated, (2) the fact that flow measurement was performed before the operation of an autoregulatory mechanism, and (3) basic differences in the determinants of "autoregulatory" mechanisms in the right ventricle compared to the left ventricle. The first possibility can be excluded because there was a significant increase in the slope of the perfusion pressure-flow relation along with increased resting flow after PA banding, suggesting that the right ventricular vasculature was not maximally vasodilated without PA banding. Support for this view is provided by studies using the micropipette technique (Gold and Bache, 1982), in which acute, severe, right ventricular pressure overload was associated with an increase in regional myocardial blood flow. An increase in slope of the pressure-coronary flow relation in studies using an electromagnetic flowmeter (Cross, 1962), corresponded to the lower limit of "autoregulatory' mechanisms (tissue pressure, myogenic factors, and metabolic influences) (Johnson, 1964) remains to be clarified.

The inflection point of the curvilinear relation between perfusion pressure and contractile force was considered as the limit of autoregulatory reserve by Downey (1976). Although the inflection point of the curvilinear relation between right coronary perfusion pressure and regional wall motion was easy to detect in RV normotension and hypertension, it was difficult to determine the inflection point between perfusion pressure and coronary flow in the present study, especially during right ventricular hypertension. Thus, the presence of an inflection point between perfusion pressure and regional wall motion suggests that this level of pressure and flow corresponds to the lower limit of "autoregulatory" reserve in the right ventricular wall, but we cannot state this with certainty.

Clinical Implications

Low output syndrome occurs in only a small percentage of patients with right ventricular infarction, because hemodynamic changes after the obstruction of the right coronary artery are usually less than those seen in cases of myocardial infarction of the left ventricle (Sharpe et al., 1978; Lorell et al., 1979). This minor influence on systemic as well as pulmonary pump performance was clearly evidenced in the present study by the physiologically insignificant changes in right and left ventricular pressures during severe coronary underperfusion.

With regard to regional wall motion, the present study clearly showed that the critical perfusion pressure of the right coronary artery was significantly below that of the left ventricle (Wyatt et al., 1975; Banka et al., 1977; Koyanagi, 1979). Since regional mechanical performance was well preserved down to the critical perfusion pressure, the right ventricular free wall may be more resistant to the effects of coronary stenosis (flow restriction) than the left ventricular free wall.

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INDEX TERMS: Coronary perfusion pressure • Autoregulation • Right ventricle • Regional ventricular function
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Y Urabe, H Tomoike, K Ohzono, S Koyanagi and M Nakamura

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