Influences of localized aortic valve damage on coronary artery blood flow in acute aortic regurgitation: an experimental study

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ABSTRACT We examined the influences of localized aortic valve damage on coronary artery blood flow and the prognosis in acute aortic regurgitation. Aortic regurgitation was produced in 18 open-chest dogs by extensively cutting one of the three aortic cusps with a nerve knife introduced via the cardiac apex. The dogs were separated into three groups of six dogs each. In each group the noncoronary cusp (NCC), the right coronary cusp (RCC), or the left coronary cusp (LCC) was cut. Aortic and left ventricular pressures; the phasic aortic, left anterior descending (LAD), and right coronary artery (RCA) blood flows; and electrocardiograms were simultaneously recorded before and after production of acute AR. All dogs in the NCC and RCC groups survived for at least 30 to 60 min, but all dogs in the LCC group died after 5 to 9 min of production of acute AR due to left ventricular failure. After 2 min of aortic regurgitation, the total, systolic, and diastolic LAD flows were 39 ± 14, 19 ± 9, and 20 ± 8 ml/min (mean ± SD) in the NCC group, 41 ± 15, 31 ± 9, and 10 ± 6 ml/min in the RCC group, and 9 ± 5, 19 ± 5, and −10 ± 2 ml/min in the LCC group, respectively. The corresponding RCA flows were 19 ± 9, 15 ± 6, and 4 ± 3 ml/min in the NCC group, 13 ± 8, 21 ± 12, and −8 ± 4 ml/min in the RCC group, and 14 ± 4, 19 ± 4, and −5 ± 1 ml/min in the LCC group, respectively. Total LAD and RCA flows decreased significantly after aortic regurgitation in the LCC and RCC groups (p < .001 and p < .05, respectively). Retrograde coronary artery blood flow was observed throughout diastole in the LAD of the LCC group and in the RCA of the LCC and RCC groups. Cardiac output and aortic systolic pressure decreased significantly after production of aortic regurgitation in the LCC group but did not change in the NCC and RCC groups. Aortic end-diastolic pressure was significantly lower in the LCC group than in the NCC and RCC groups after aortic regurgitation. There were no significant differences among the three groups in the regurgitant fraction, cardiac output, left ventricular end-diastolic pressure, aortic systolic pressure, or heart rate. These results suggest that in dogs with acute aortic regurgitation (1) prognosis is remarkably poor when aortic regurgitation is caused by a damaged LCC and (2) left or right coronary artery blood flow is significantly decreased when the corresponding cusp is damaged.


THE PROGNOSIS in patients with acute aortic regurgitation is generally poor because early death due to left ventricular failure is frequent despite intensive medical management. Hemodynamic features of severe acute aortic regurgitation have been reported previously,1,2 and the effects of acute aortic regurgitation on the coronary blood flow have been studied in dogs.3–7 No attention, however, has been paid to the influences of localized aortic valve damage. The purpose of this study was to examine the effects of localized aortic valve damage on right and left coronary artery blood flows and the prognosis of acute aortic regurgitation in the dogs.

Methods

Eighteen mongrel dogs weighing 14 to 21 kg were anesthetized with sodium pentobarbital intravenously (25 mg/kg) and were ventilated with room air. A midsternal thoracotomy was performed and the pericardium was cut. Micromanometer-tipped catheters were positioned in the ascending aorta from the right carotid artery and in the left ventricle from the cardiac apex to measure the aortic and left ventricular pressures. Flow probes
were positioned on the ascending aorta, proximal left anterior descending artery (LAD), and right coronary artery (RCA) and were connected to electromagnetic flowmeters (Nihon-Koden MFV 1200) to measure aortic, LAD, and RCA blood flows. The pericardium was then closed. The coronary blood flow zero value was checked by occlusion at a portion distal to the flow probe. Dogs were monitored electrocardiographically (lead II) throughout the experiment. Control measurements were simultaneously recorded. The apex portion of the pericardium was cut, and aortic regurgitation was produced by extensively cutting one of the three aortic cusps with a nerve knife via the cardiac apex.\(^8\)\(^9\) Immediately after production of aortic regurgitation, the pericardium was closed. All measurements were done continuously for 30 to 60 min, and reported values represent data averaged from at least 5 beats. Calculations of aortic and coronary blood flows were made as described by Folts and Rowe.\(^4\) Aortic cusp damage was confirmed at necropsy in all dogs. The dogs were separated into three groups of six dogs each, with lesions of the noncoronary cusp (NCC), the right coronary cusp (RCC), or the left coronary cusp (LCC).

Comparison of data between control and aortic regurgitation in each of the three groups was made with the paired \(t\) test. Comparison of data among the three groups was made by an appropriate multiple-sample comparison test (two-way analysis of variance, followed by unblocked Newman-Keuls test). Data were considered significant at the \(p < .05\) level. Measurements are reported as mean \(\pm SD\).

Results

All six dogs in the LCC group died after 5 to 9 min of production of aortic regurgitation due to left ventricular heart failure. All 12 dogs in the NCC and RCC groups survived for more than 30 min after aortic regurgitation. The lead II electrocardiogram showed marked ST depression in all six dogs of the LCC group. In contrast, no ST depression or elevation was observed in all 12 dogs of the NCC and RCC groups (figures 1 through 3).

Hemodynamic data from the control state and after 2 min of aortic regurgitation are shown in table 1. In the control state there were no significant differences among the three groups in all hemodynamic variables.

After 2 min of aortic regurgitation, aortic systolic pressure and cardiac output decreased in the LCC group (both \(p < .05\)) but did not change in the NCC and RCC groups. In all three groups, aortic end-diastolic pressure decreased and the left ventricular end-diastolic pressure elevated significantly. Heart rate did not change in each of the three groups after creation of aortic regurgitation. Aortic end-diastolic pressure was significantly lower in the LCC group than in the NCC and RCC groups (\(p < .001\) and \(p < .05\), respectively). Aortic regurgitant fraction was 51 \(\pm 16\%\) (range 30\% to 71\%) in the NCC group, 56 \(\pm 9\%\) (range 41\% to 64\%) in the RCC group, and 53 \(\pm 11\%\) (range 36\% to 67\%) in the LCC group (figure 4). There were no significant differences among the three groups in heart

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**FIGURE 1.** Representative tracings of the left anterior descending coronary artery flow (LADF), right coronary artery flow (RCAF), aortic flow (AoF), and electrocardiogram (ECG) in the control state and 2 min after creation of aortic regurgitation (AR) from one dog in which the NCC was extensively cut. An arrow shows the retrograde RCA flow during end-diastole S = systolic; D = diastolic.
rate, aortic systolic pressure, left ventricular end-diastolic pressure, cardiac output, forward aortic flow, regurgitant aortic flow, and regurgitant fraction after aortic regurgitation.

Total LAD flow decreased remarkably from $31 \pm 10$ ml/min in control to $9 \pm 5$ ml/min ($p < .001$) after aortic regurgitation in the LCC group but did not change in the NCC and RCC groups. Systolic LAD flow increased significantly after aortic regurgitation in all three groups. Diastolic LAD flow decreased significantly in the RCC and LCC groups (both $p < .001$). Retrograde LAD flow throughout diastole was observed in all six dogs of the LCC group (figure 3) but was not observed in the NCC and RCC groups.

Total RCA flow decreased from $18 \pm 8$ ml/min in control to $13 \pm 8$ ml/min after aortic regurgitation ($p < .05$) in the RCC group but did not change in the NCC and LCC groups. Systolic RCA flow was increased significantly in all three groups. Diastolic RCA flow decreased significantly in the RCC and LCC groups (both $p < .01$). Retrograde RCA flow throughout diastole was observed in all dogs of the RCC and LCC groups but was not observed in the NCC group.

Total and diastolic LAD flows were significantly lower in the LCC group than in the remaining groups (figure 5). There was no significant difference in total RCA flow among the three groups. Diastolic RCA flow was significantly lower in the RCC and LCC groups than in the NCC group (both $p < .001$).

The fraction of the coronary blood flow during systole was different during control and aortic regurgitation. The systolic fraction of the LAD and RCA flows in the NCC group increased from $21 \pm 5\%$ to $48 \pm 11\%$ ($p < .01$) and from $50 \pm 10\%$ to $80 \pm 7\%$ ($p < .001$).
FIGURE 3. Representative tracings of the left anterior descending coronary artery flow (LADF), right coronary artery flow (RCAF), aortic flow (AoF), and electrocardiogram (ECG) in the control state and 2 min after creation of aortic regurgitation (AR) from one dog in which the LCC was extensively cut. Black arrows show retrograde LAD and RCA flows throughout diastole. White arrow shows marked ST depression on the ECG. S = systolic; D = diastolic.

.01) during aortic regurgitation, respectively. The systolic fraction of the LAD flow in the RCC group increased from 22 ± 4% to 79 ± 8% (p < .01) during aortic regurgitation. There was no correlation between the systolic fraction of the coronary blood flow and the aortic regurgitant fraction in the NCC and RCC groups, respectively.

Discussion

The effects of acute aortic regurgitation on the coronary blood flow in dogs have been reported previously, but the effects of localized aortic valve damage have not been evaluated. Our results showed that the LAD and RCA flows and the prognosis were significantly different among the three groups studied. Whereas all dogs in the NCC and RCC groups survived more than 30 min after aortic regurgitation, all dogs in the LCC group died within 9 min due to left ventricular failure. Both total LAD and RCA flows did not change in the NCC group after aortic regurgitation. Total LAD flow did not change and total RCA flow decreased in the RCC group. Total LAD flow decreased remarkably and total RCA flow did not change in the LCC group. A negative diastolic LAD flow was measured in the LCC group and a negative diastolic RCA flow was observed in both the LCC and RCC groups. From these findings, the cause of early death in the LCC group may have been severe ischemia resulting from a marked decrease in the LAD flow suggested by marked ST depression on the electrocardiogram. In the dogs, whereas the right coronary artery perfuses the bulk of the outer wall of the right ventricle, the left coronary artery perfuses the entire left ventricular free wall and septum.

The phenomenon of the retrograde coronary blood flow during diastole in aortic regurgitation has been reported previously. In experimental studies, Folts and Rowe used intact dogs and found that as AR became
severe (aortic regurgitant fraction 53% to 68%), retrograde coronary blood flow occurred during diastole and the net diastolic coronary blood flow became near zero or negative. They produced aortic regurgitation with a valve-spreading catheter that could spread all three aortic cusps. This retrograde flow pattern is similar to that in the RCC and LCC groups in our study (figures 2 and 3). Aortic regurgitant fraction, however, ranged widely from 36% to 67% in the RCC and LCC groups in the present study. Feldman et al. observed retrograde flow during end-diastole in one dog with severe aortic regurgitation produced with a valve-spreading catheter. In clinical studies, Carroll and Falsetti reported that retrograde flow during end-diastole evaluated by coronary angiograms, was observed in six of the eight patients with pure aortic regurgitation. We also observed a similar retrograde flow during end-diastole as shown in figure 1. Folts et al. measured phasic right coronary blood flow in patients with aortic regurgitation at the time of surgery before and after repair of aortic regurgitation. They observed a significant increase in the diastolic/systolic coronary blood flow ratio after the aortic valve had been repaired but did not mention retrograde coronary flow.

The mechanism that produces retrograde coronary blood flow during diastole is not clear. From our re-
results, some explanation for the phenomenon of the retrograde flow throughout diastole may be possible (figure 6). There were no significant differences in aortic regurgitant fraction and left ventricular end-diastolic pressure among the three groups. In the NCC group, the retrograde flow throughout diastole did not occur in the left coronary artery (LCA) and RCA when the LCC and RCC were intact, and the aortic diastolic pressure was not remarkably low. In the RCC group, the retrograde flow occurred in the RCA and did not occur in the LCA when the RCC was cut. Regurgitant stream flow near the ostium of the RCA results in the Venturi effect, which may alter the RCA flow. However, we did not measure the pressures at both ostia of the LCA and RCA. In the LCC group, retrograde flow occurred in both the LCA and RCA when the LCC was cut and aortic diastolic pressure became markedly low. A combination of the Venturi effect and low coronary perfusion pressure may affect both LCA and RCA flows. Our data suggest that a normal aortic cusp adjacent to the ostium of the coronary artery has an important function: keeping the blood flow of the coronary artery antegrade during diastole.

Several limitations of this study should be emphasized. First, since we assessed the prognosis and hemodynamic variables in aortic regurgitation with an extensively damaged cusp, we have no data on the effect of a partially damaged aortic cusp. Second, myocardial perfusion was not measured in this study. Further studies may be needed to evaluate the effect of retrograde coronary blood flow during diastole on myocardial perfusion.

FIGURE 5. Comparison of total and diastolic LAD and RCA flows after 2 min of aortic regurgitation among the NCC, RCC, and LCC groups. Mean values ± 1 SD are shown by the open circles and horizontal bars.

FIGURE 6. Schematic diagrams of aortic and left and right coronary blood flows, shown by white arrows, during diastole in the three groups. Ao = aorta; LV = left ventricle.
The area perfused by the left coronary artery in humans is different from that in dogs. In humans, the left coronary artery perfuses the major area of the left ventricle except for the posterior portion of the interventricular septum. Therefore, our results may suggest that the prognosis in patients with an extensively damaged LCC in acute aortic regurgitation may be poor and that prompt surgical intervention is indicated for these patients. Echocardiography may be useful in the detection of a damaged aortic cusp in a large percentage of patients with acute aortic regurgitation and may assist the clinician in determining whether prompt surgery is indicated.

The mechanism of angina pectoris in patients with chronic aortic regurgitation and normal coronary arteries is not clear. Decreased blood flow of the coronary artery situated on the damaged cusp may explain angina pectoris in some patients with aortic regurgitation. We have sometimes observed regional wall motion abnormalities of the left ventricle in patients with chronic aortic regurgitation, but the degree of damage on each of the three aortic cusps may not be equal in such patients. Unequal damage on aortic cusps may produce different degrees of reduced blood flows during diastole in the LCA and RCA, which may be one of the possible causes for regional wall motion abnormalities in these patients.

We conclude that in dogs with acute aortic regurgitation, right and left coronary blood flows are influenced differently by damage of the right, left, or noncoronary cusp and that prognosis is remarkably poor when the left coronary cusp is damaged in contrast to when the right or noncoronary cusp is damaged.

References
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