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Abstract

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KEYWORDS: stenotic resistance, reactive hyperemia, distal coronary pressure

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INCREASE IN STENOTIC RESISTANCE FOLLOWING A BRIEF CORONARY OCCLUSION IN THE ANESTHETIZED OPEN-CHEST DOG

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Abstract. Changes in the stenotic resistance of a coronary artery following brief coronary occlusion were studied in the anesthetized open-chest dog. A critical coronary stenosis was constructed by tying a thick string around the circumflex coronary artery (LCx) near its origin. The LCx was occluded for 5, 10, 15, 20 and 30 seconds with and without coronary stenosis, then the reactive hyperemia was observed. In the absence of the stenosis, resistance of the segment of the large coronary artery remained unchanged during the reactive hyperemia independent of the duration of the occlusion. In the presence of the stenosis, however, stenotic resistance increased for a certain time after the release of occlusion. This increased resistance lasted longer with more severe stenosis and with longer duration of coronary occlusion. These results suggest that stenotic resistance can increase dynamically, and that the duration of increased resistance may reflect the severity of the stenosis.

Key words : stenotic resistance, reactive hyperemia, distal coronary pressure.

Brief coronary occlusion causes intense coronary vasodilation and a marked increase in flow. The presence of coronary stenosis decreases the flow response to the vasodilatory stimuli: the capacity to increase flow over resting basal levels in response to a stimulus disappears with constriction of 88 to 93 % of arterial diameter (1). Traditionally, coronary artery stenoses are considered as fixed, passive lesions that do not respond to vasoactive stimuli. However, recently, coronary artery spasm associated with atherosclerotic lesions has been documented (2). In addition, ergonovine-induced coronary spasm usually occurs near sclerotic lesions (3, 4). Maseri *et al.* (5) have shown from studies of postmortem heart that diseased stenotic regions often contain arterial wall segment which appear normal and able to contract. These studies imply that certain diseased coronary arteries constrict at the site of atherosclerotic plaques, suggesting a dynamic mechanism with changing severity of obstruction.

This study investigates whether the resistance of a stenotic segment of coro-

nary artery changes following momentary interruption of coronary flow, and whether the changes in stenotic resistance are affected by the duration of this interruption of flow.

METHODS

Twenty-three mongrel dogs of either sex weighing 10-18 kg were premedicated with ketamine hydrochloride, then anesthetized with 30 mg/kg of pentobarbital sodium. Respiration was controlled to maintain blood gases wihtin normal ranges by volume adjustment and supplemental oxygen. The left circumflex coronary artery was isolated near its origin through a left thoracotomy. An electromagnetic flow transducer and pneumatic cuff occluder were placed around the vessel. A thick cotton string (diameter 1.0 mm, length 3 cm) for producing coronary stenosis was loosely positioned around the vessel between the flow transducer and the cuff. A small (outer diameter 1.5 mm, length 10 cm), polyethylene, end-hole catheter was inserted into a small branch of the circumflex coronary artery distal to the cuff. This catheter was used for recording coronary pressure distal to the constrictor and the pressure is hereafter called the distal coronary pressure. Neither the flow transducer nor the coronary catheter affected control and maximum coronary flow or induced significant pressure gradients. A hard polyethylene catheter was inserted into the ascending aorta through the left carotid artery for monitoring systemic blood pressure.

Experimental protocol was as follows. After baseline flow was recorded, the circumflex coronary (LCx) was occluded for 15 seconds by inflating the pneumatic cuff and the hyperemic response was recorded. The coronary catheter was then inserted and reactive hyperemia to a 15-second occlusion was repeated in order to verify that this catheter did not impair the flow response. Experimental runs were made when the artery was unconstricted and at the degree of coronary obstruction which nearly eliminated reactive hyperemia. After stabilization, coronary occlusions for 5, 10, 15, 20 and 30 seconds were made and then the artery was constricted with the cotton string to the degree described above: peak reactive hyperemia flow (PRH) showed less than 130% of the preocclusion flow. After 5 min to establish the new steady state of coronary flow and distal coronary pressure, coronary occlusions for 5, 10, 15, 20 and 30 seconds were repeated. The order of the occlusion duration was completely randomized and 5 min was allowed the hemodynamic situation to stabilize between each coronary occlusion. Following completion of these steps, the constrictor was removed and flow allowed to stabilize. The flow response to a 15-second occlusion was measured again for comparison with the pre-experimental response in order to demonstrate stability and responsiveness of the myocardium. If either the baseline flow or the PRH in the post-experimental period differed by more than 10% from the values during the pre-experimental preiod, the data from the dog were excluded. All data were continuously recorded on a Siemens-Elema Mingograph Model 804 recorder at paper speeds from 2.5 to 100 cm per second, and mean values of pressures and flow were analyzed. Stenotic resistance was calculated as the pressure gradient across the stenosis divided by the mean coronary flow. To clarify the lingering effects of each coronary occlusion on stenotic resistance, the time for distal coronary pressure to return to 80% of the preocclusion level was measured.

RESULTS

Heart rate and systemic blood pressure were not changed significantly by

coronary occlusion during either control period or during coronary stenosis. In the absence of coronary constriction the pressure gradient between in the ascending aorta and in the distal branch of the circumflex coronary artery was less than 6 mmHg before coronary occlusion. The vascular resistance in large coronary arteries (R_L) was approximately 3% of the total resistance of the circumflex coronary bed (R_T): R_L was calculated as the pressure gradient between the ascending aorta and the branch of the coronary artery divided by coronary flow. Transient coronary occlusion was followed by a marked excess flow above the preocclusion level. Peak flow during reactive hyperemia increased progressively with an increase in the duration of coronary occlusion and reached a maximum with a 15- or 20-second coronary occlusion. The distal coronary pressure returned to the preocclusion level quickly following the occlusion, though the longer occlusion tended to cause slower recovery. As a result, reactive hyperemia did not essentially affect the R_L independent of occlusion time (Fig. 1, left), while resistance of small coronary arteries in the circumflex coronary bed (R_S) decreased from a baseline level of 1.32 ± 0.19 mmHg/ml/min/100 g (mean $\pm$ SD) to 0.39 ± 0.093 mmHg/ml/min/100g at peak reactive hyperemia following a 15-second coronary occlusion, where R_S was calculated as the distal coronary pressure divided by coronary flow. This resulted in a marked fall in R_T.

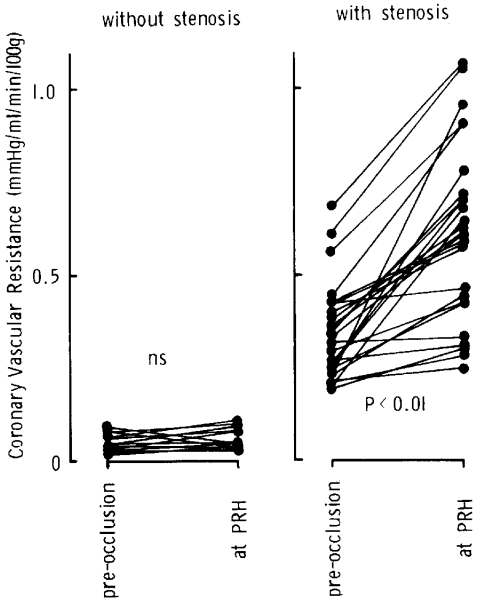

Fig. 1. Resistance of large coronary artery segment at pre-occlusion period and peak reactive flow following a 15-second coronary occlusion with (right) and without (left) coronary constriction. PRH = peak reactive hyperemia.

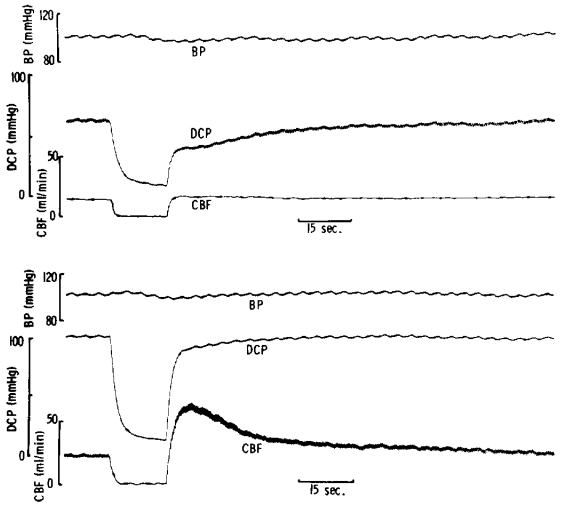

Fig. 2. Typical responses of blood flow and distal coronary pressure to a 15-second coronary occlusion in the presence (upper) and the absence (lower) of coronary constriction. With coronary constriction, persistent fall in distal coronary pressure was noted following the release of occlusion. BP = aortic pressure, DCP = distal coronary pressure, CBF = coronary blood flow in the circumflex coronary artery.

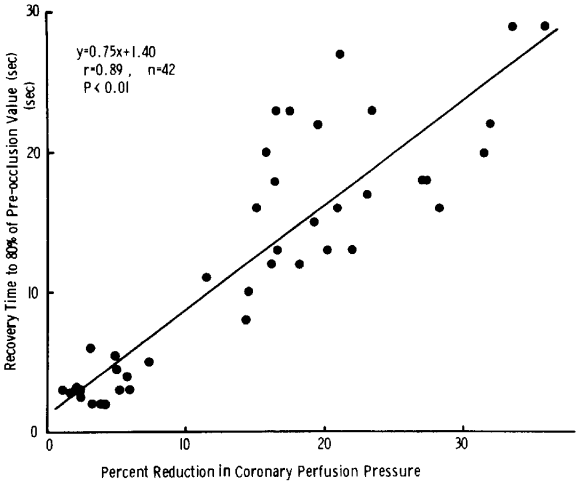

Fig. 3. Relationship between percent reduction in distal coronary pressure caused by 15-second coronary occlusions and recovery time for the pressure to 80% of the pre-occlusion level.

With coronary constriction, baseline coronary flow decreased slightly but significantly from 88 ± 18.3 ml/min/100g (mean ± SD) to 82 ± 26.9 ml/min/100g ($P < 0.01$). The distal coronary pressure fell significantly from 98 mmHg to 77 mmHg ($P < 0.01$). The percent drop in coronary perfusion pressure, which was calculated as the distal coronary pressure after constriction divided

by that before constriction, varied in the range of 12% to 36% by the degree of constriction. Coronary constriction increased R_L to approximately 20% of R_T in the circumflex coronary bed. After the release of the coronary occlusion, the coronary flow quickly returned to the preocclusion level independent of the occlusion time and the magnitude of the pressure gradient. On the contrary, slow recovery of the distal coronary pressure followed a rapid initial rise approximately to 65% of the preocclusion pressure. Fig. 2 represents typical records of the flow and pressure responses to a 15-second occlusion with (upper) and without (lower) coronary constriction, and Fig. 1, right, shows R_L with coronary constriction before coronary occlusion and at PRH following 15-second coronary occlusions. While R_L at PRH varied widely, all of 23 experiments indicated a significant increase in R_L at PRH in comparison with preocclusion R_L.

Recovery of the distal coronary pressure was progressively slower with increases in the percent drop in coronary perfusion pressure and with a prolongation of occlusion time. To verify the slow recovery, the time for the distal coronary pressure to return from the beginning of the reflow to 80% of the preocclusion level (T_{80}) was measured and analyzed. A close linear relationship was observed between the percent drop in coronary perfusion pressure and T_{80} as shown in Fig. 3 which was obtained from the experiments of 15 second occlusions. Moreover, the slope of the line became steeper along with an increase in occlusion time as shown in Fig. 4.

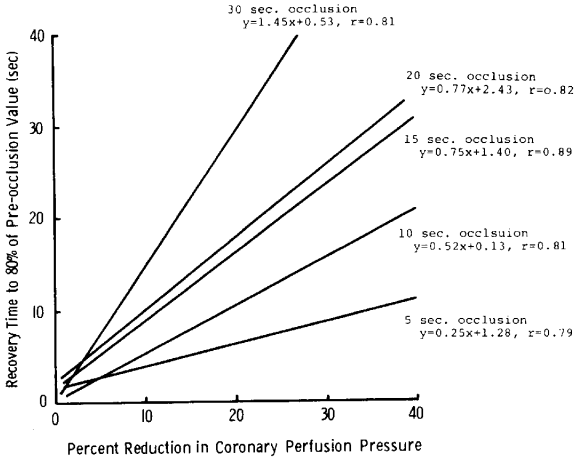

Fig. 4. Relationship between precent reduction in distal coronary pressure and recovery time for the pressure to 80% of pre-occlusion levels following 5-, 10-, 15-, 29- and 30-second coronary occlusions. The slope becomes progressively steeper with increase in occlusion duration.

DISCUSSION

In this study, the following two consclusions were made: firstly, stenotic resistance created by external constriction increased flow following brief occlusion of the coronary artery. Secondly, persistence of this increased resistance was progressively more pronouncod after occlusions of longer duration and with stenosis of more severe obstruction.

Without coronary constriction, marked increases in coronary blood flow followed by brief coronary occlusion in the absence of significant changes in the resistance of the large coronary artery segment; distal coronary resistance alone decreased markedly. In the presence of coronary stenosis at a degree of constriction that caused no substantial reactive hyperemia, stenotic resistance increased significantly after brief coronary occlusion, then distal coronary pressure gradually returned to the control level. It has previously been shown that as flow across a stenosis increases, calculated resistance increases (6). Gould *et al.* (7) reported in 1975 that coronary stenotic resistance increases as coronary flow increased. Logan (8) demonstrated in postmortem perfused human hearts that stenotic resistance increased during a decrease in distal coronary pressure. However, since in our study the increase in resistance across the stenotic segment was associated with essentially constant flow, marked flow change alone is an unlikely reason for the increase in stenotic resistance. Santomore and Walinsky (9) have proposed that the reduction in distal or intraluminal coronary pressure known to occur after administration of coronary vasodilators, either with or without an increase in coronary flow, causes mechanical collapse of the wall of the stenotic segment of coronary artery. On the contrary, Brown (10) and Doemer and colleagues (11) reported consistent increases in the cross-sectional area of coronary stenosis after administration of coronary vasodilators in man and corresponding marked decrease in stenotic resistance derived from stenotic geometry. Whatever the mechanism concerned, an increment in resistance actually occurs after the application of a brief stress.

Although it is difficult to extrapolate from animal experimets to the clinical condition of human patients, it is reasonable to apply some of our results to patients since the relationship of flow to pressure reflects fundamental physical principles. Schwartz and his coworkers (12) using ventricular pacing in anesthetized open-chest dogs, reported that the fall in distal coronary pressure and the increase in stenotic resistance tended to persist after cessation of pacing tachycardia. Clinically, Lepeschkin and Surawicz (13) reported that in most cases with coronary heart disease, significant depression of the ST-segment in the ECG lasted for 3 min or longer after stopping the exercise. It has also been stated that the electocardiographic ST-segment depression persisted less than 2 min in normal persons, but longer 3 min in patients with coronary insufficiency (14). All these results including ours suggest that, in the presence of severe coronary stenosis, the recovery time from stress-induced abnormalities may be a useful

marker of the severity of the coronary stenosis. In our study, the time progressively increased in association with prolongation of occlusion period, hence ischemic abnormalities were easier to detect, the longer the stree was continued.

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