Acta Medica Okayama

Volume 34, *Issue* 2 1980 *Article* 4

APRIL 1980

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Abstract

The effects of changes in distal resistance on stenotic resistance were studied in vitro. Physiological saline was passed through the left carotid artery obtained from the dog, flexible rubber tubing, or through solid polyethylene tubing with a constant perfusion pressure or with a constant flow rate. Various stenotic resistances were established using a screw type constrictor and the distal resistance was varied by allowing physiological saline to pass through either a 23 gauge hypodermic needle (high peripheral resistance) or 23 and 20 gauge needles (low peripheral resistance). For arteries with anatomically fixed stenosis, the calculated resistance was increased in association with reduction of the distal resistance. The stenotic resistance in the flexible rubber tubing changed in the same manner as that of the carotid artery, while the solid polyethylene tubing showed no significant stenotic resistance changes due to altering the distal resistance. These findings suggest that the stenotic resistance change of the artery correlates with the elasticity of the vessel wall and also indicate that resistance values were of little usefulness for evaluating the effects of vasodilating stimuli on the vessel segment with a significant stenosis.

KEYWORDS: stenotic resistance, constant perfusion pressure, constant flow rate.

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*PMID: 6450512 [PubMed - indexed for MEDLINE]

Acta Med. Okayama **34**, (2), 109—115 (1980)

INCREASE IN THE CALCULATED RESISTANCE OF ANATOMICALLY FIXED STENOSIS IN VITRO IN ASSOCIATION WITH DECREASE IN DISTAL RESISTANCE

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Received February 21, 1980

Abstract. The effects of changes in distal resistance on stenotic resistance were studied *in vitro*. Physiological saline was passed through the left carotid artery obtained from the dog, flexible rubber tubing, or through solid polyethylene tubing with a constant perfusion pressure or with a constant flow rate. Various stenotic resistances were established using a screw type constrictor and the distal resistance was varied by allowing physiological saline to pass through either a 23 gauge hypodermic needle (high peripheral resistance) or 23 and 20 gauge needles (low peripheral resistance). For arteries with anatomically fixed stenosis, the calculated resistance was increased in association with reduction of the distal resistance. The stenotic resistance in the flexible rubber tubing changed in the same manner as that of the carotid artery, while the solid polyethylene tubing showed no significant stenotic resistance changes due to altering the distal resistance. These findings suggest that the stenotic resistance change of the artery correlates with the elasticity of the vessel wall and also indicate that resistance values were of little usefulness for evaluating the effects of vasodilating stimuli on the vessel segment with a significant stenosis.

Key words: stenotic resistance, constant perfusion pressure, constant flow rate.

The stenotic resistance of the coronary artery is generally calculated by the following equation, according to Ohm's law:

stenotic resistance = pressure gradient across the stenosis/flow.

This equation is available for evaluating the stenotic resistance when the conducting tube is rigid and inflexible, and the flow is laminate (1). The vessel is, however, highly elastic and it is well known that post-stenotic blood flow is not laminate but turbulent.

The area of a vessel is related to the intraluminal pressure: increase in the intraluminal pressure will increase the vessel area, while a decrease in intra-

luminal pressure will decrease the vessel area (2, 3). Decrease in the vessel area will result in an elevation of flow resistance. Post-stenotic pressure should be influenced by the peripheral resistance. Therefore, it is suggested that changing the peripheral resistance may alter the stenotic resistance. The present paper investigates *in vitro* the effect of the peripheral resistance change on the resistance of anatomically fixed stenosis.

METHODS

Constant perfusion pressure experiment. The experimental system is illustrated schematically in Fig. 1.

A 35 mm length of left carotid artery was rapidly removed after killing a dog, then was put into chilled physiological saline until it was studied. The experiment was completed within 3 h of removing the artery. In the study, the artery was attached to hard polyethylene tubings (2.65 mm in the internal diameter, 3.65 mm in the external diameter and 350 mm in the length) at points A and B, and stretched to its original length. The artery was kept moist by externally applying warm (37°C) physiological saline. Pressures were measured just proximal (P1) and distal (P2) to the artery with Statham pressure transducers. Physiological saline passed through the artery and then either through a 23 gauge hypodermic needle (high peripheral resistance, high PR) or 23 and 20 gauge hypodermic needles (low peripheral resistance, low PR). To maintain P1 (proximal pressure = perfusion pressure) constant, air was blown into 500 ml triangle flask filled with 400 ml physiological saline through a rubber stopper (see Fig. 1). Using a screw type constrictor

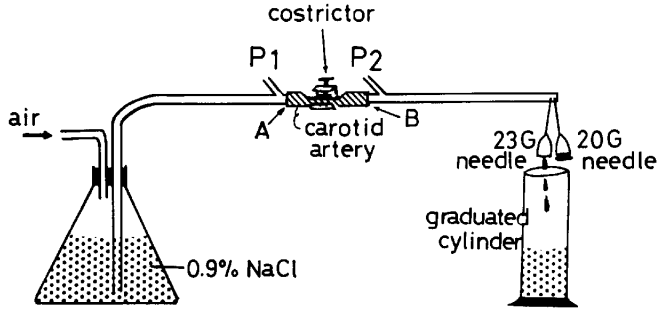

Fig. 1. Schematic illustration of the constant perfusion pressure system. The carotid artery was attached to polyethylene tubes at points A and B. Pressures were measured just proximal (P1) to, and distal (P2) to, the artery.

(10 mm in the length), various stenotic resistances were established, with a high PR (23 gauge needle). Without or with the value of stenotic resistance set and the pressures recorded, the stopcock was opened allow flow through both the 23 and the 20 gauge needles (low PR). P1 and P2 were recorded. Physiological saline was collected through the needle (or needles) into a graduated cylinder.

To elucide the role of the stenosis itself in the pressure-flow relationship, the

artery was replaced with either an elastic (thin wall rubber tubing, external diameter 4.0 mm, internal diameter 3.5 mm, length 35 mm) or an inflexible tubing (polyethylene tubing, external diameter 2.65 mm, internal diameter 1.25 mm, length 35 mm), and the above procedure was repeated.

Constant flow rate experiment. A constant flow system was the same as the one used in the constant perfusion pressure experiment except a Harvard syringe pump was used instead of a saline-filled flask and air jet. The flow rate was kept constant at 9.89 ml·min^{-1} (Fig. 2).

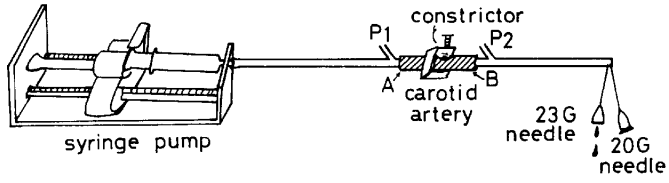

Fig. 2. Schematic illustration of the constant flow rate system. The carotid artery was attached to polyethylene tubes at points A and B. The flow rate was kept constant at 9.89 ml·min^{-1} with a Harvard syringe pump.

The same procedure described in the constant pressure experiment was repeated with a constant flow rate instead of the constant perfusion pressure. P1 and P2 were recorded.

The stenotic resistance was calculated from the following equation; stenotic resistance (mmHg·ml^{-1}·min^{-1}) = (P1–P2)/F, where P1 and P2 are proximal and distal pressures (mmHg), respectively, and F is the flow rate (ml·min^{-1}) of physiological saline.

Statistical analysis were performed with paired Student's t-test.

RESULTS

Constant perfusion pressure experiment. Table 1 summarises the results obtained with a constant perfusion pressure.

Without stenoses, a pressure gradient between P1 (proximal) and P2 (distal) was not observed regardless of the level of the peripheral resistance in any of the experimental materials; arteries, rubber or polyethylene tubings.

For the carotid artery (12 observations in 3 arteries) with a stenosis, however, decreasing the peripheral resistance always caused the stenotic resistance to increase. The average stenotic resistance with the low PR calculated was three (severe stenosis) or four (mild stenosis) times greater than the one with the high PR. This increase in the stenotic resistance resulted from a marked reduction in the distal pressure and a slight elevation in the flow rate. The stenotic resistance change with change in the peripheral resistance was also observed in elastic thin wall rubber tubing, but not in inflexible hard polyethylene tubing. The magnitude of the stenotic resistance changes were less in the rubber tubing than in the carotid artery.

TABLE 1. CONSTANT PERFUSION PRESSURE EXPERIMENTS

	Pressure (mmHg)		Flow (ml. min^{-1})	Stenotic resistance (mmHg. ml^{-1}. min^{-1})	
	Proximal	Distal			
Carotid artery					
a) without stenosis					
high PR	165±0.5	165±6.8	34.8±3.1	0.01±0.02	
low PR	164±1.8	163±5.2	53.7±4.3	0.01±0.003	
b) with severe stenosis					
high PR	160±1.1	140±6.4	10.1±2.3	1.97±0.05	**
low PR	160±1.3	38±3.2	20.2±2.6	60.5±0.09	
c) with mild stenosis					
high PR	150±0.9	148±7.1	12.5±1.3	0.16±0.001	**
low PR	150±1.1	124±6.8	38.5±3.4	0.69±0.02	
Thin wall rubber tube					
a) without stenosis					
high PR	150±0.9	150±1.0	40.5±4.1	0.01±0.003	
low PR	150±1.1	150±1.5	64.5±6.1	0.01±0.04	
b) with severe stenosis					
high PR	150±1.3	90±5.4	20.5±3.3	2.90±0.14	**
low PR	150±2.2	58±4.9	14.8±4.3	3.96±0.22	
c) with mild stenosis					
high PR	155±2.7	140±3.8	37.8±4.0	0.40±0.02	*
low PR	155±4.3	106±6.2	41.5±3.3	1.02±0.04	
Hard polyethylene tube					
a) without stenosis					
high PR	160±1.8	159±2.5	45.3±4.4	0	
low PR	160±2.5	156±3.4	91.1±5.9	0	
b) with severe stenosis					
high PR	160±1.8	96±5.5	22.7±5.0	3.07±0.12	
low PR	160±3.6	30±3.2	50.7±4.9	2.76±0.33	
c) with mild stenosis					
high PR	150±1.2	146±4.9	22.1±2.4	0.18±0.04	
low PR	150±1.4	133±5.6	88.5±6.1	0.19±0.07	

high PR=high peripheral resistance, low PR=low peripheral resistance.
Statistically significant difference in the stenotic resistance between high and low peripheral resistance, ** $R<0.01$, * $P<0.05$.

Constant flow rate experiment. The results obtained from the constant flow experiment are summarised in Table 2.

Without stenoses, the resistance of either carotid arteries, the rubber or inflexible polyethylene tubings measured was almost zero under conditions of

both high PR and low PR.

With the severe stenosis used in this study, however, the stenotic resistance increased by approximately 25 percent with a reduction in the peripheral resistance, which decreasing the peripheral resistance caused the stenotic resistance to rise markedly in mild stenosis. The increase in the stenotic resistance calculated in association with decreasing the peripheral resistance resulted from a marked reduction in the distal pressure accompanied with a slight or no change in the proximal pressure.

TABLE 2. CONSTANT FLOW (9.89 ML. MIN^{-1}) EXPERIMENTS

	Flow rate (ml. min^{-1})	Pressure (mmHg)		Stenotic resistance (mmHg. ml^{-1}. min^{-1})	
		Proximal	Distal		
Carotid artery					
a) without stenoses					
high PR	9.89	110±4.9	109±5.5	0.10±0.09	
low PR	9.89	21±1.8	21±2.6	0.02±0.13	
b) with severe stenosis					
high PR	9.89	258±20.5	31±11.9	23.41±5.86	*
low PR	9.89	252±26.3	10±6.0	29.36±10.61	
c) with mild stenosis					
high PR	9.89	150±11.8	107±17.4	4.32±1.00	**
low PR	9.89	148±13.1	20±3.8	12.90±2.34	
Thin wall rubber tube					
a) without stenoses					
high PR	9.89	106±10.8	106±11.2	0.00±0.03	
low PR	9.89	52±5.3	51±4.9	0.05±0.02	
b) with stenosis					
high PR	9.89	152±9.4	60±4.8	8.86±3.21	**
low PR	9.89	124±11.6	16±4.4	11.01±4.23	
Hard polyethylene tube					
a) without stenoses					
high PR	9.89	110±6.7	109±8.1	0.09±0.05	
low PR	9.89	19±2.0	17±4.1	0.11±0.06	
b) with stenosis					
high PR	9.89	140±8.9	114±10.3	2.83±0.96	
low PR	9.89	48±3.7	19±2.1	2.92±0.55	

high PR=high peripheral resistance, low PR=low peripheral resistance.

Significant difference in the stenotic resistance between the two levels of the peripheral resistance, ** $P<0.01$, * $P<0.05$.

With changing the peripheral resistance, the thin wall rubber tubing altered the stenotic resistance in the same manner as the carotid artery. On the other

hand, no significant changes in the stenotic resistance were observed in the polyethylene tubing following a reduction in the peripheral resistance.

DISCUSSION

The present study indicates that the calculated stenotic resistance, which is anatomically fixed, of the carotid artery markedly increased in association with decreasing the peripheral resistance in the experiments of constant perfusion pressure and constant flow rate. Several possible mechanisms for the observed increase in stenotic resistance were considered; flow turbulence, wall elasticity, surface profile and friction, and others. Flow turbulence through the stenosis could cause an increase in stenotic resistance (4). However, similar stenotic resistance changes were not observed in inflexible polyethylene tubing suggesting that flow turbulence is unlikely as the primary cause of the change in stenotic resistance observed in carotid arteries. The internal surface of the carotid artery, the flexible rubber tubing and the inflexible polyethylene tubing is intact and smooth, so it, too, is an unlikely friction force causing the changes observed in stenotic resistance.

In dogs with stenosis severe enough to abolish reactive hyperemia, the distal pressure falls to persistently low levels after transient occlusion, according to Schwartz *et al.* (5) and Walinsky *et al.* (6). The present results agree with their reports.

Changes in stenotic resistance occurred in flexible rubber but not in stiff polyethylene tubing, indicating that wall elasticity is an important factor. The most plausible explanation of the increase in stenotic resistance is a change in the geometery of the stenosis. A change in the lumen area at, or just distal to, the stenosis could explain the large increase in stenotic resistance in association with a decrease in the peripheral resistance. A fall in the distal pressure accompanied the increase in stenotic resistance. By Bernouilli's equation and direct measurement, the coronary pressure decrease caused a reduction in the pressure at the stenosis (7). We postulate that the distal pressure fall caused a decrease in the lumen area at the stenosis. Gould *et al.* (4) showed *in vivo* that the anatomically fixed stenosis resistance increased in association with increasing flow rate through the stenosis. The stenotic resistance, however, was increased with decrease in the peripheral resistance, not only during constant perfusion pressure but also during the constant flow rate experiment. Cannon *et al.* (8), Logan *et al.* (9), Shipley and Gregg (10), and Fiddian *et al.* (11) have shown *in vivo* that the extent of flow reduction varied in inverse relation to the changes in the peripheral resistance of the vascular bed and the lumen areas of the stenosis. The present study confirms their findings, and further suggests that the stenotic resistance changes correlate with the elasticity of the vessel wall.

Since Fam and McGregor (12) reported the effects of certain drugs on large coronary arteries utilizing resistance values derived from the flow and the pressure gradient across the stenosis, many investigators have studied stenotic resistance changes using this method (13-15). As mentioned above, however, stenotic resistance values calculated by this method were altered in association with changes in the peripheral resistance, even in anatomically fixed stenosis. Therefore, the present results indicate that resistance values were of little usefulness for evaluating the effects of drugs on vessel segments with significant stenosis when the drug has an apparent dilating effect on the peripheral vascular bed.

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