Regional Blood Flows and Resistances in Conscious One-Kidney, One-Clip Renovascular Hypertensive Rats

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Abstract Three regional blood flows were measured in one-kidney, one-clip renovascular hypertensive (one-kidney hypertensive) rats with chronically implanted electromagnetic flow probe. One-kidney hypertensive rats showed about 30% greater superior mesenteric flow, about 20% greater hindquarter flow at the terminal aorta, and an almost unchanged renal flow at the clipped renal artery when compared with control rats, but the sum of the mean values of these three regional blood flows in one-kidney hypertensive rats was almost the same as that of control rats. One-kidney hypertensive rats had a higher peripheral resistance in all the investigated vascular areas. The increase in peripheral resistance of the renal area including the clipped and removed arteries was greater than that in peripheral resistance of the superior mesenteric area or hindquarter area. These findings suggest that the remaining renal area which failed to compensate for the flow deprived by uni-nephrectomy plays a role in the etiology of this kind of hypertension.

Key words: renovascular hypertension, peripheral resistance, renal flow, splanchnic flow, muscle flow.

For a better understanding of the characteristics of hypertension it is important to ascertain the hemodynamics of hypertension. In many kinds of hypertension, cardiac output at the resting state is within the normal range, but the total peripheral resistance is elevated almost proportionally to arterial pressure (Freis, 1960; Olmsted and Page, 1965; Ledingham and Pelling, 1967; Ferrario, 1974; Ferrario and Page, 1978; Teranishi and Iriuchijima, 1983).

Is the elevation of total peripheral resistance due to a uniform elevation of peripheral resistance in various parallel vascular regions or to a marked elevation of peripheral resistance in a special vascular bed? The results of our previous studies using an electromagnetic flow probe showed that peripheral resistance was not uniformly increased but a marked increase in peripheral resistance was observed in
the superior mesenteric area of two-kidney, one-clip renovascular hypertensive (two-kidney hypertensive) rats (TERANISHI and IRIUCHIJIMA, 1985) and in the hindquarter area of spontaneously hypertensive rats (SHR) (IRIUCHIJIMA, 1983).

The aim of the present study was to investigate in one-kidney hypertensive rats how the cardiac output is distributed to various regional vascular areas and where the increase in peripheral resistance is marked in various vascular beds. Regional flows were measured at the superior mesenteric area, hindquarter area and renal area with clipped kidney in this kind of hypertensive rats with chronically implanted electromagnetic flow probe.

MATERIALS AND METHODS

Induction of experimental hypertensive rats. Male Wistar rats 10-20 weeks in age were used in the present study. To produce one-kidney, one-clip renovascular hypertension, the rats were anesthetized by intraperitoneal injection of 50 mg/kg of thiamylal sodium, and a metal tape 1 mm in width and 0.1 mm in thickness with a gap of 0.3 mm was retroperitoneally inserted into the renal artery by a flank incision. The contralateral kidney and renal artery were removed.

Implantation of flow probe and catheter. Two to 4 weeks after applying the clip, blood pressure was measured indirectly by the tail-cuff method in order to confirm that the rats were hypertensive. In the hypertensive rats, an electromagnetic flow probe (Nihon Kohden, Tokyo) was implanted at a superior mesenteric artery (internal diameter: 1.5 mm), at a clipped renal artery (0.8 or 1.0 mm) or at a terminal aorta (2.0 mm) under anesthesia with 50 mg/kg of thiamylal sodium. The details of the employed technique have been reported previously (KAWAUE and IRIUCHIJIMA, 1984). In all the rats with a flow probe implanted except the ones at the terminal aorta, a catheter was inserted from the femoral artery to the abdominal aorta for direct measurement of arterial pressure. As controls, a flow probe was implanted and a catheter was inserted in Wistar rats of the same age.

Measurement. After probe implantation and catheter insertion, the rats were placed separately in a white polyethylene cage containing wood chip and given ample pellets and drinking water. After allowing 2 or more days for recovery, the regional blood flows and arterial pressure were recorded continuously until a resting value was obtained. The heart rate was measured by occasionally speeding up the pen-writing recorder while recording the flows. The rat was judged to be in a steady state from its outward appearance.

Statistical analysis. Student’s t-test was employed for statistical analysis and $p < 0.05$ was used to imply statistical significance.

RESULTS

A representative example of recorded arterial pressure (AP), superior mesenteric flow (SMF), renal flow (RF), and hindquarter flow (HQF) at the terminal
aorta in the hypertensive state (left) and in the control state (right) is shown in Fig. 1. Each blood flow was obtained from different animals.

**Renal flow**

Renal flow was measured at the clipped artery in hypertensive rats and at an intact renal artery in control rats. The mean values of renal flow and other parameters at the resting state in hypertensive rats and control rats are shown in Table 1. The mean value of the renal flow of the hypertensive rats was not significantly different from the corresponding value of control rats.

**Superior mesenteric flow**

As shown in Table 2, the mean value of superior mesenteric flow and other parameters at the resting state obtained from hypertensive rats were significantly higher than the corresponding values from control rats. The mean flow of the hypertensive rats was about 30% greater than that of control rats. Figure 2, shows the relationship between arterial pressure and superior mesenteric flow. The superior mesenteric flow increased in proportion to arterial pressure in hypertensive rats ($r = 0.458$, $p < 0.001$).

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**Fig. 1.** Example of recording of arterial pressure (AP), superior mesenteric flow (SMF), renal flow (RF), and hindquarter flow (HOF) in conscious one-kidney, one-clip renovascular hypertensive rats (left) and normal control rats (right). Arterial pressure was recorded simultaneously with superior mesenteric flow in one rat and the others in different rats. Renal flow was measured at the clipped artery in a hypertensive rat and at an intact artery in a normal control rat.

Vol. 38, No. 1, 1988
Hindquarter flow at the terminal aorta

As it is not possible to insert a catheter in measuring hindquarter flow, the blood pressure of hypertensive rats was measured indirectly by the tail-cuff method before implanting the flow probe. The mean value of the blood pressure from 13 hypertensive rats was 205 ± 23.5 mmHg. The mean hindquarter flow was 6.59 ± 0.87 ml/(min · 100 g) in 13 hypertensive rats (body weight: 296 ± 30.6 g) and was 5.43 ± 0.73 ml/(min · 100 g) in 21 control rats (body weight: 294 ± 43.4 g). The

Table 1. Comparison of renal flow and other parameters between one-kidney, one-clip renovascular hypertensive rats and normal control rats.

|                      | Hypertensive rats (n=9) | Normal rats (n=11) | p <  
|----------------------|------------------------|--------------------|------
| Arterial pressure (mmHg) | 173 ± 29.1             | 115 ± 8.17         | 0.001 |
| Heart rate (beats/min) | 368 ± 42.9             | 339 ± 22.8         | N.S. |
| Renal flow (ml/(min · 100 g)) | 2.43 ± 0.40          | 2.46 ± 0.62        | N.S. |
| Renal resistance (mmHg · min · 100 g/ml) | 74.0 ± 22.3       | 50.3 ± 16.1        | 0.02 |
| Body weight (g)         | 319 ± 50.0             | 312 ± 31.6         |      |

Mean ± S.D. Renal flow was measured at the clipped artery in hypertensive rats and at the intact artery in normal control rats.

Table 2. Comparison of superior mesenteric flow and other parameters between one-kidney, one-clip renovascular hypertensive rats and normal control rats.

|                      | Hypertensive rats (n=14) | Normal rats (n=20) | p <  
|----------------------|------------------------|--------------------|------
| Arterial pressure (mmHg) | 176 ± 14.1             | 111 ± 9.71         | 0.001 |
| Heart rate (beats/min) | 376 ± 40.3             | 349 ± 28.8         | 0.05 |
| Superior mesenteric flow (ml/(min · 100 g)) | 6.43 ± 1.33          | 4.99 ± 0.61        | 0.001 |
| Superior mesenteric resistance (mmHg · min · 100 g/ml) | 28.7 ± 7.33          | 22.5 ± 3.46        | 0.01 |
| Body weight (g)         | 291 ± 48.1             | 287 ± 38.0         |      |

Mean ± S.D.
The regional blood flows in renal, superior mesenteric, and hindquarter areas. The flow at the clipped renal artery in one-kidney hypertensive rats was unchanged from the corresponding value of control rats. According to Shimamoto and Iriuchijima (1987), who measured the flow at the remaining renal artery of DOCA-salt hypertensive and uni-nephrectomized rats with electromagnetic flowmeter, the renal flow of these rats increased more than twofold that of normal rats. It is suggested from their observation that the clipped renal artery in one-kidney hypertensive rats could not compensate for the flow deprived by uni-nephrectomy.

One-kidney hypertensive rats had a greater flow superior mesenteric area and in hindquarter area. The magnitude of the increase was about 30% in superior mesenteric area and was about 20% in hindquarter area which consists of the major
parts of the skeletal muscle area in the hind limb. Such a great regional blood flow has not been observed in two-kidney hypertensive rats with a decreased superior mesenteric flow (Teranishi and Iriuchijima, 1985) nor in SHR with a decreased hindquarter flow (Iriuchijima, 1983). DOCA-salt hypertensive and normotensive uni-nephrectomized rats had an increased superior mesenteric flow and a normal hindquarter flow (Shimamoto and Iriuchijima, 1987). But, superior mesenteric resistance obtained in one-kidney hypertensive rats was greater than that obtained in DOCA-salt hypertensive or normotensive uni-nephrectomized rats. For calculation of hindquarter resistance, the mean value of arterial pressure recorded with superior mesenteric flow was substituted. The hindquarter resistance was almost equal between one-kidney hypertensive rats and DOCA-salt hypertensive rats. The value of hindquarter resistance obtained in two types of hypertensive rats was also greater than that obtained in uni-nephrectomized rats. It is suggested from these findings that the greater superior mesenteric and hindquarter flows observed in one-kidney hypertensive rats may be not related to uni-nephrectomy but related to a special characteristic associated with development of this type of hypertension.

**Regional contribution to hypertension.** In the established phase of one-kidney hypertensive rats, elevation of arterial pressure was mainly attributable to elevation of total peripheral resistance and the increase in cardiac output played a relatively minor part (Ledingham and Pelling, 1967; Ferrario and Page, 1978). In the present study, one-kidney hypertensive rats had significantly higher peripheral resistances in all the investigated vascular areas compared with those in control rats (see Table 1 and 2). However, as shown in Fig. 2, superior mesenteric flow increased in proportion to elevation in arterial pressure. A similar situation was also observed in hindquarter flow, but the flow at the clipped renal artery was unchanged with elevation of arterial pressure. These findings indicate that the elevation of resistance was uniformly distributed in various parallel vascular areas and that the vascular area with marked elevation in resistance was the renal area.

In one-kidney hypertensive rats, Flohr et al. (1976), using particle-distribution techniques under light ether anesthesia, have reported that the increase in skeletal muscle resistance was significantly greater than that in total peripheral resistance, and that the increase in resistance in splanchnic area was less than that in total peripheral resistance. The disagreement between their results and ours is assumed to be due to the difference in the methods employed. This assumption was supported by Kawaue and Iriuchijima (1984) who reported that the distribution of regional blood flows was changed by pentobarbital anesthesia in normal rats for 30 min after pentobarbital injection. The increase in hindquarter resistance was greater than that in total peripheral resistance while superior mesenteric resistance decreased in the face of the increase in total peripheral resistance.

Charocoilos et al. (1984), using radioactive microspheres, reported that in one-kidney hypertensive rats the vascular resistance was greatly elevated in the gastrointestinal tract, muscle, and skin. In their studies, however, the heart rate was 10–40% greater than that of ours and the sympathoadrenal system seemed to be
excited by stress accompanying the injection of radioactive microspheres. We have observed previously that excitation of the sympathoadrenal system resulted in an increase in heart rate and in superior mesenteric resistance (Teranishi et al., 1985).

In the present study, the rats were unrestrained and almost free to move. The condition of the present experiment allowed us to record the regional blood flows directly and continuously for a long time. Therefore it can be assumed that our data reflect the condition at the resting state of hypertension.

It can be concluded that one-kidney hypertensive rats are characterized by an increased superior mesenteric flow, an increased hindquarter flow and an unchanged renal flow at the clipped artery. It may be the renal area that contributes markedly to the increase in total peripheral resistance and that the renal area failed to compensate for the flow deprived by uni-nephrectomy.

REFERENCES


