Relationship between Systolic Arterial Pressure and Heart Mass in the Rat

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SUMMARY

This study describes the relationship between left ventricular mass and systolic arterial pressure (SAP) in normotensive and hypertensive rats. The genetically hypertensive rats (SHR) were stratified according to their SAP values in to hypertensive (SHRH) and normotensive (SHRN) subgroups. Males and females of both subgroups exhibited biventricular hypertrophy and the left ventricular mass was not correlated with SAP values. An overall cardiac enlargement was also found in female rats of the normotensive WKY group. In DOCA-salt and 2K/1C hypertensive rats the left ventricular mass was correlated positively with SAP. These data suggest that SAP is not a factor in the development of left ventricular hypertrophy in the SHR strain, however, they also revealed a right ventricular mass increase in this strain with respect to the Wistar strain. (Jpn Heart J **34**: 795–801, 1993)

Key Words:

Hypertension Left and right ventricular mass SHR strain WKY strain Mineralocorticoid hypertension Renal hypertension

SEVERAL lines of evidence support the hypothesis that the heart hypertrophy found in the SHR strain is not related to heritable systemic arterial hypertension.[1)–4)] Rats of SHR-Wistar hybrid strains in our laboratory also show increases in heart mass that appear to be unrelated to a pressure overload effect.[5),6)] This study has used a larger sample of SHRs to determine the relationship between mass of the right and left ventricles and systolic arterial pressure. Since 15% of males and 68% of female rats from the SHR strain of the local colony included in this study did not exhibit arterial hypertension, they were stratified into normotensive (SHRN) and hypertensive (SHRH) subgroups. Mineralocorticoid plus salt overload (DOCA-salt) and renal (2K/1C) hypertensive rats were also used to test the impact of acquired hypertension on ventricular mass. Normotensive rats of the Wistar and Wistar-Kyoto strains were used as controls. Values of the measured ventricular mass in all groups studied were

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referred to a calculated value for each ventricular mass; this value was obtained from the correlation of ventricular weights with body weights carried out with female and male rats of the Wistar strain.

Methods

Wistar, WKY and SHR strain rats were bred under the same care and environmental conditions, and maintained on a standard rat diet and tap water ad libitum.

Three groups of hypertensive rats were studied:

1. Genetically hypertensive (SHRH) group: Rats of the Aoki-Okamoto strain (66 males and 27 females).

2. Renal hypertensive (2K/1C) group: Hypertension was induced by placing a silver clip (0.22 mm internal diameter) on the left renal artery of Wistar rats under ether anesthesia (18 males and 8 females).

3. Mineralocorticoid hypertensive (DOCA-salt) group: Hypertension was induced in unilaterally nephrectomized Wistar rats (8 males and 5 females) by weekly subcutaneous administration of 20 mg of deoxycorticosterone acetate (Sigma) dissolved in sesame oil (200 mg/ml). The animals' water supply consisted of tap water containing 1% NaCl and 0.2% KCl. Rats were used 4 weeks after induction of hypertension.

Three groups of normotensive rats were also studied:

1. Wistar normotensive (W) group: This group included sham operated rats (controls for 2K/1C rats and unilaterally nephrectomized rats). Salt was added to the drinking water of controls for DOCA-salt rats. This group contained 98 males and 57 females.

2. Wistar-Kyoto normotensive (WKY) group: Control rats for the SHR strain (14 males and 13 females).

3. SHR normotensive (SHRN) group: Rats of the SHR strain that did not exhibit an increase in systolic arterial pressure (22 males and 60 females).

Systolic arterial pressure (SAP) was measured weekly from the caudal artery of unanesthetized rats with the tail-cuff plethysmographic method. The value of SAP used to correlate with the ventricular mass values was the average of two measurements performed during the week in which the animal was sacrificed. Prior to sacrifice, the rats were weighed and anesthetized with sodium pentobarbital. The heart was removed immediately and placed in saline. The left ventricle, including the interventricular septum, was dissected from the right ventricle. Ventricles were washed with saline, blotted and weighed.

Assessment of ventricular mass modifications was carried out as follows: Regression equations for ventricular weight versus body weight were obtained

Table I: Regression Equations for Ventricular Weights and Body Weight of Normotensive Rats

	Equation to obtain mass (g) of:		r
Female right ventricle	0.0161+0.5116×BW	(n=46)	0.7989
Female left ventricle	0.0690+1.6494×BW	(n=46)	0.9397
Male right ventricle	0.0347+0.4677×BW	(n=77)	0.7859
Male left ventricle	0.0969+1.6327×BW	(n=77)	0.9079

BW=body weight (Kg); r=correlation coefficient; n=number of rats.

from data of 77 males and 46 females of the Wistar strain. Table I presents the equations derived with the corresponding correlation coefficient values. Using the sex-matched equation for each ventricle, the value of body weight of each rat (normotensive or hypertensive) allowed the calculation of the corresponding ventricular weight value. The difference between this predicted ventricular weight and the actual ventricular weight was expressed as a percentage of the former. The means of the percentage deviations were compared among groups by one-way analysis of variance using the Peritz' F test.[7] The statistical significance level was set at $P<0.05$.

Results

The body weights of WKY, SHRH, SHRN and experimentally hypertensive Wistar rats were compared to body weight curves of normotensive Wistar rats from the local colony (Fig. 1). A consistently lower body weight was

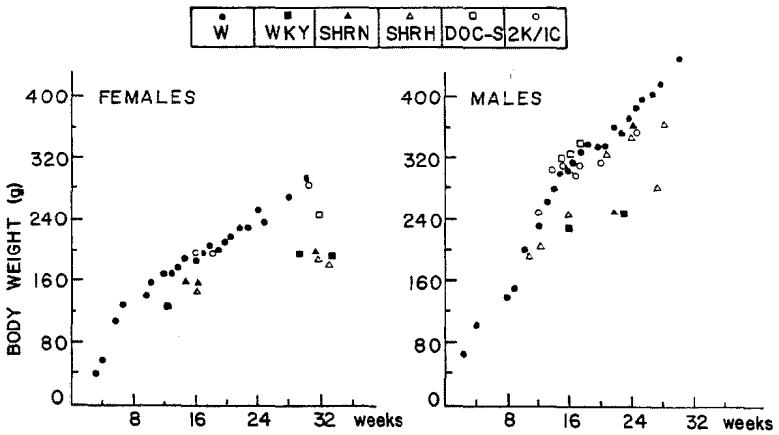

Fig. 1. Body weights (g) of female and male Wistar rats from 2 to 28 weeks old. Body weight values (means for each week) of normotensive (WKY and SHRN) and hypertensive (SHRH, DOCA-salt and 2K/1C) rats are indicated by symbols shown on the top of the Figure. For each week of age, points represent mean of body weights; standard errors are not visible because the size of the symbols exceeds their values. The total number of Wistar rats whose body weight was measured to obtain the curve of normal growth in this strain was 503 for males and 425 for females.

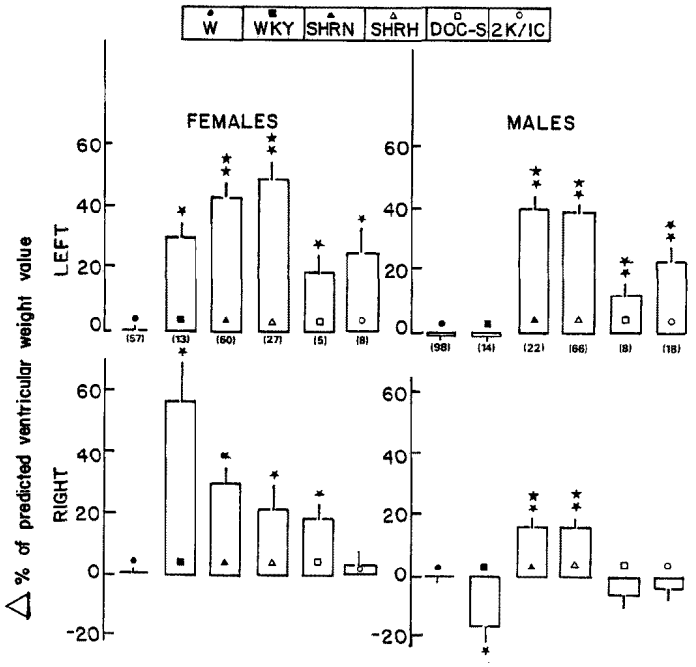

Fig. 2. Percent deviations of left ventricular weight from its predicted values derived from regression equations (see Table I). Bars show mean values of the variable with indication of the SEM. Number of animals is indicated within brackets for each group. *indicates $P<0.05$ with respect to the Wistar group and **with respect to both Wistar and WKY groups.

found in the WKY and SHR rats with respect to the Wistar strain, but no differences were detected between the WKY and SHR strains. Wistar rats from DOCA-salt and 2K/1C hypertensive groups did not differ significantly in their body weight values from those of the Wistar control group; however, DOCA-salt female rats had lower body weights than sex-age-matched Wistar rats.

Figure 2 illustrates the percentage deviations of ventricular mass for all the groups studied with respect to the normotensive Wistar strain rats (SAP: 123±2 and 127±1 mmHg for females [F] and males [M], respectively). Both female and male rats of the SHR groups (SAP for SHRN: 127±2 [F] and 122±6 mmHg [M]; SAP for SHRH: 171±3 [F] and 186±3 mmHg [M]) showed a 40–50% increase in their left ventricular mass and a 15–30% increase in their right ventricular mass. These values were still valid for male rats of the SHR groups compared with the male WKY strain rats (SAP: 134±5 mmHg). However, due to the fact that female WKY strain rats (SAP: 122±4 mmHg) exhibited biventricular hypertrophy, only the increase in left ventricular mass remains significant in females of the SHR groups although this increase was reduced to about 15%.

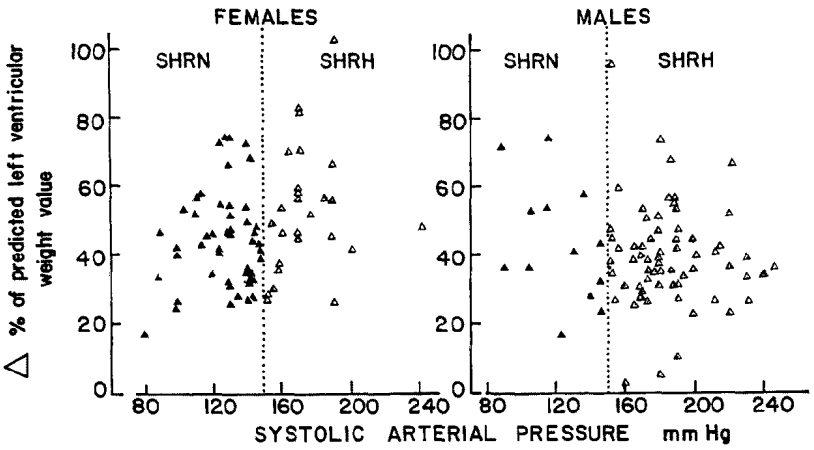

Fig. 3. Relationship between values of percent deviation of left ventricular weight and systolic arterial pressure. Correlation coefficients for the different groups were: Female SHRN and SHRH: 0.1089 and 0.2247, respectively, male SHRN and SHRH: −0.4572 and 0.0904, respectively.

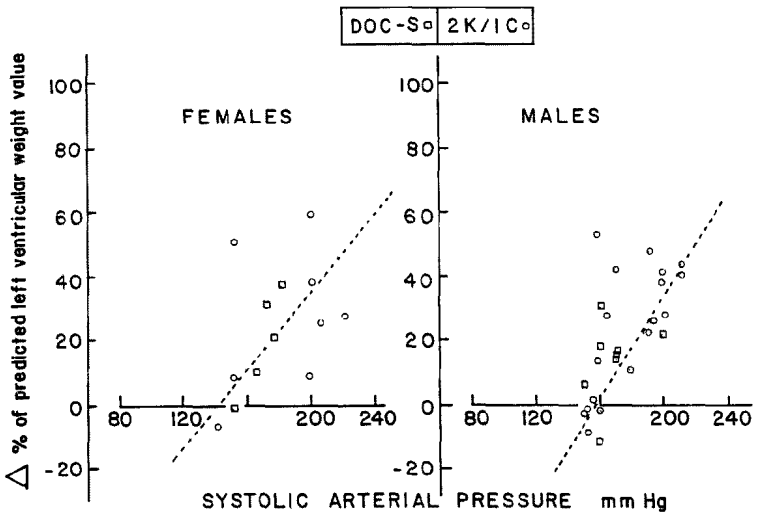

Fig. 4. Relationship between values of percent deviations of left ventricular weight from predicted values and systolic arterial pressure. Correlation coefficient for the different groups were: DOCA-salt=0.5344 and 2K/1C=0.6466 ($P<0.05$ in both cases).

The correlation between left ventricular percentage deviations and systolic arterial pressure values in normotensive and hypertensive SHR subgroups is shown in Figure 3. Low correlation coefficient values (similar to those presented in the legend of Figure 3) were obtained from analyses of the data from Wistar

rats (r=0.1643 [F] and 0.0111 [M]) and WKY rats (r=0.3515 [F]) and 0.0460 [M]).

DOCA-salt hypertensive rats (SAP: 168 ± 5 [F] and 172 ± 4 mmHg [M]) increased their left ventricular mass by 10–20%; right ventricular mass increased by 20% only in female rats (Fig. 2). Renal hypertensive rats (SAP: 183 ± 11 [F] and 179 ± 6 mmHg [M]) also increased their left ventricular mass about 20%. A significant positive correlation was obtained from the relationship between percent increases in left ventricular mass and systolic arterial pressure for the latter experimentally hypertensive groups (Fig. 4).

Discussion

In this study the mass variation of ventricles in normotensive and hypertensive rats is expressed as percentage deviations from the mass of ventricles in body weight-sex-matched normotensive Wistar rats. In principle, this method makes use of the ventricular mass to body mass relationship, similar to the ratio of those parameters that is usually employed as an index to detect ventricular hypertrophy. The equations provided by the present results allow one to calculate the mass of the right or left ventricles according to the sex and body mass of Wistar strain rats and compare the actual ventricular mass of experimental groups with those values.

The SHR strain showed an overall increase in myocardial weight with respect to the Wistar strain, independent of the levels of systolic arterial pressure. This result was equally true for left and right ventricles. A dissociation of left hypertrophy from pressure overload has been reported in SHRs[1)–6)] and in patients with mild essential hypertension.[8)] The present results show that the right ventricle mass in SHRs is 20–30% greater than in Wistar rats. There was also a marked (60%) difference in weight between the right ventricles of female WKY rats and Wistar rats, consistent with previous reports of biventricular hypertrophy in female WKY animals.[9)] A sexual dimorphism has been described in genetically hypertensive rats[10)] and in rats subjected to DOCA-salt administration.[11)] These findings indicate that female rats have both a greater degree of cardiac enlargement and less elevated systolic blood pressure than male rats.

There was no significant relationship between left ventricular weight and systolic arterial pressure in the genetically hypertensive groups. Both DOCA-salt and 2K/1C hypertensive rats showed a positive correlation between left ventricular weight and systolic arterial pressure. The hypertrophy was about half of that shown by the SHR groups, despite the fact that levels of SAP were similar in all the hypertensive groups. Thus, elevated SAP is not sufficient to explain the development of left ventricular hypertrophy in genetically hypertensive rats.

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