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Left Ventricular Hypertrophy in Early Hypertensive Children ; Its Importance as a Risk Factor for Hypertension

The Shimane Heart Study

(left ventricular hypertrophy/early-hypertension/risk factor for hypertension)

TOSHIKAZU NISHIO[a], CHUZO MORI[a], MASAKAZU SAITO[a], TAKESHI SOEDA[a], KATSUTOSHI ABE[b], and YASUJI NAKAO[b]

[a]*Department of Pediatrics, Shimane Medical University and* [b]*Shimane Prefectural Central Hospital, Izumo 693, Japan*

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Left ventricular muscle volume (LVMV) was echocardiographically measured in 296 normotensive and 12 "borderline" hypertensive children aged 6—15 years.

LVMV were enlarged in two among 12 hypertensive children. A girl aged 14 with a family history of hypertension had a markedly enlarged LVMV (145.8 ccm) despite "borderline" hypertension (132/80). Thus, left ventricular hypertrophy may have already occurred before or immediately after the development of hypertension as observed in spontaneously hypertensive rats. It was concluded that the enlarged LVMV during childhood was a risk factor for hypertension and its early detection was important for the prevention of hypertension.

The normotensive children were divided into two groups, one with a family history of hypertension and the other without. There were no differences in values of LVMV, serum cholesterol and blood pressure between the groups. Although the significant differences were not present before the age of 15, on-going follow-up studies are expected to provide more pertinent information.

Recent experimental observations in spontaneously hypertensive rats indicate that morphological and/or physiological changes due to hypertension originate early in life, (1, 2). It seems reasonable that the analogous changes may occur in human beings before or immediately after the hypertension is clinically diagnosed. If the changes could be detected during childhood, the prevention of hypertension could be considered when the subject is at the pediatric level.

For these purposes, an extensive survey of children, "the Shimane Heart Study", was commenced in Shimane Prefecture from the spring of 1978. We report herein the left ventricular muscle volume (LVMV) of both normotensive and hypertensive children, and the relationship between the family history of hypertension and the values of blood pressure, serum cholesterol, and LVMV. Normal values of LVMV and serum cholesterol in children were detailed in previous reports (3, 4).

MATERIALS AND METHODS

1. Study Population

Two hundred and ninety-six primary school (6—10 years) and junior high school (12—15 years) children were studied in the spring of 1978. Details of the study population are shown in Table I. The families of almost all the children have resided in Shimane Prefecture for generations. Family history of apoplexy, hypertension, coronary heart diseases, obesity, and diabetes mellitus was taken, and apoplexy in the family was chosen as the most reliable risk factor related to hypertension.

In addition, 12 children of hypertension, so diagnosed at Shimane Prefectural Central Hospital were included in the study.

Table I. *Number of Subjects*

Age (yrs)	Sex	Family history of apoplexy (+)	(−)
6— 7	Male	17	58
	Female	12	31
9—10	Male	18	30
	Female	9	33
12—15	Male	11	30
	Female	14	33
Total		81	215

2. Examination

The following examinations were performed : anthropometric measurements (body weight, height, chest circumference, upper arm circumference, skinfold thickness), physical examinations, blood pressure measurements, hemoglobin and serum cholesterol determinations, and urinalyses. Body surface area was estimated from body weight and height by nomogram.

Blood pressure was measured in the left arm by mercury sphygmomanometer. The cuffs used were 9 cm in breadth for 6—10 year-old children and 12 cm for children over the age of 12 years. Systolic and diastolic pressures were recorded at the onset of phase I and phase IV in sounds of Korotkoff, respectively.

Electrocardiograms of both standard 12 leads and X Y Z component of Frank lead system were taken and put on magnetic tapes for computer analysis.

Echocardiography was done utilizing a transducer with a frequency of 3.5 MHz for younger children and 2.25 MHz for older children. Ultrasonoscope and echocardiogram recorder were Fukuda Denshi SSD-110S type and ECO-125S type, respectively.

3. Quantitative Evaluation of Echocardiogram

The left ventricular echocardiogram was recorded when the ultrasound

passed through the left ventricle where the left ventricular dimension was maximal and the following structures were well visualized : anterior and posterior mitral leaflets, tendinous cords or papillary muscles, endocardial surfaces of both interventricular septum and left ventricular free wall, and epicardium posterior to the left ventricular wall. Thickness of both the interventricular septum(IVST) and the left ventricular posterior wall(LVPWT), and the maximal left ventricular internal dimension (LVID) were obtained.

The landmarks for measurement were so selected that dense echoes of the endocardium were included in IVST and LVPWT, and that LVID was from the posterior border of interventricular septal endocardium to the anterior border of left ventricular posterior wall (the "Standard convention (5, 6)").

These measurements were made at the phase of end-diastole, practically at the peak of R wave of electrocardiogram simultaneously recorded. Thus, these values were abbreviated IVSTd, LVPWTd, and LVIDd, repsectively.

The left ventricular muscle volume (LVMV) was estimated by the method of Troy *et al.* (7) with some modification (3). The formula used was :

$$LVMV = 1.05\,(LVIDd + IVSTd + LVPWTd)^2\left[LVIDd + 1/2\,(IVSTd + LVPWTd)\right] - 1.05\,(LVIDd)^3$$

RESULTS

1. Clinical Evaluation of Hypertensive Children

Clinical data of the hypertensive children are shown in Table II. Cases from No.1 to No.8 are essential hypertension or hypertension without renal disease. Cases from No.9 to No.12 are secondary hypertension or hypertension with renal disease.

Table II. *Clinical Data of Hypertensive Children*

Case No.	Age	Sex	Diagnosis	Blood pressure		LVMV
				At the time of echo-examination	Maximum during course	
1	9	f	Essential hypertension	132/84	?	80.8
2	9	f	〃	136/84	?	102.7
3	10	f	〃	148/98	?	111.4
4	12	m	〃	166/72	168/68	116.8
5	14	f	〃	132/80	?	145.8
6	14	f	〃	126/60	140/80	75.4
7	14	m	〃	134/60	172/98	102.8
8	14	m	〃	146/65	?	156.8
9	14	m	Renal hypertension (renovascular disease)	128/70	166/100	163.2
10	15	m	Renal hypertension (chronic nephritis)	136/90	154/96	96.7
11	16	f	Renal hypertension (SLE-nephritis)	130/80	180/102	85.5
12	10	f	Secondary hypertension (drug related)	124/56	146/60	62.4

2. Left Ventricular Muscle Volume (LVMV) of Hypertensive Children

Values of LVMV in hypertensive children are illustrated in Fig. 1 by cross marks in comparison with those of normotensive children. Five among the 12 hypertensive children had a markedly enlarged LVMV. These included 4 with essential hypertension (No.2, 3, 5, 8) and one with secondary hypertension and renal disease (No.9).

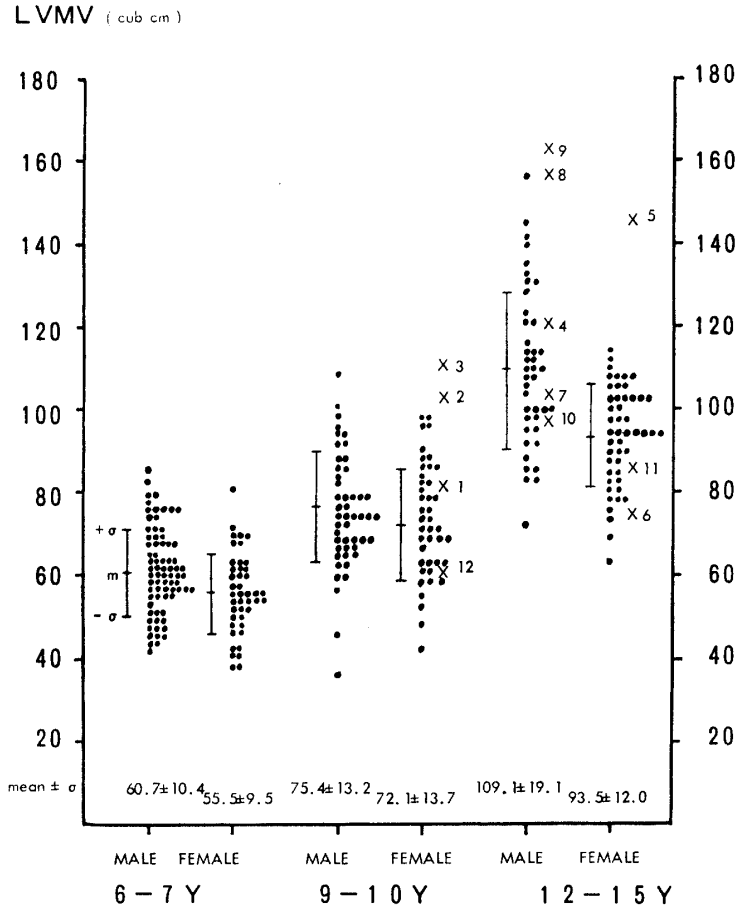

Fig. 1. LVMV of hypertensive (×) and normotensive (●) children.

3. LVMV Plotted against Body Surface Area (BSA) in Hypertensive Children (Figs.2 and 3)

LVMV was plotted against BSA in order to rule out the influence of variations in BSA. Thus, 2 children(No.5 and No.9) were interpreted to have a markedly enlarged LVMV in comparison with the values of normotensive children.

Case No.5 (Figs. 3, 4) was a 14-year-old girl of "borderline" hypertension (132/80) without renal disease. She was considered to have left ventricular hypertrophy, as the LVMV was 145.8 ccm. In this patient, the left ventricle was markedly hypertrophied in spite of hypertension of "borderline" level. Her paternal grandmother had hypertension.

Case No.9 (Figs. 2, 5) was a 14-year-old boy with hypertension (166/100)

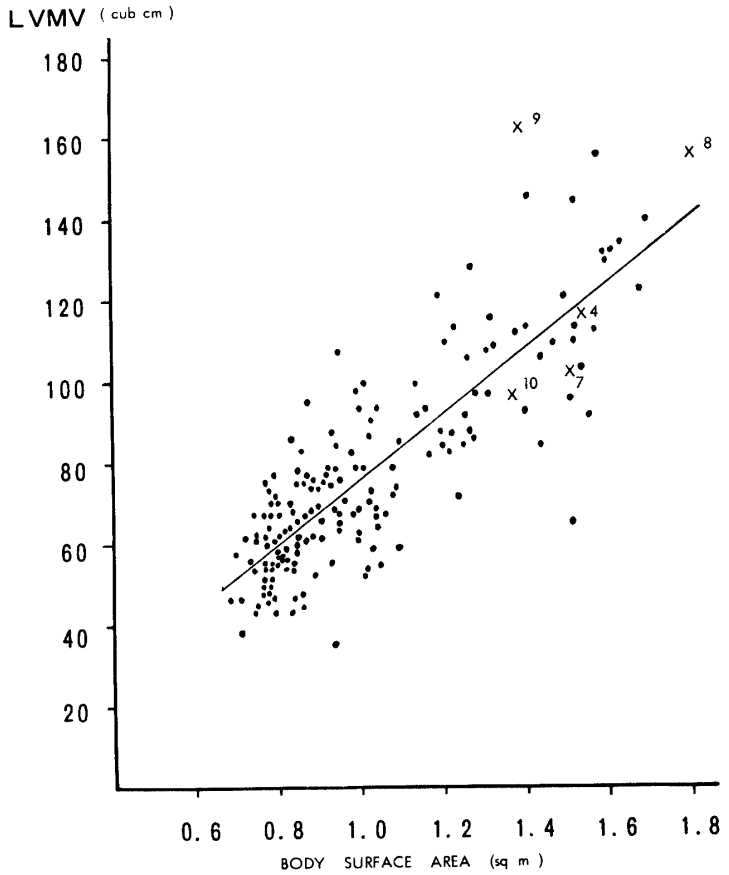

Fig. 2. LVMV plotted against body surface area in hypertensive (×) and normotensive (●) boys.

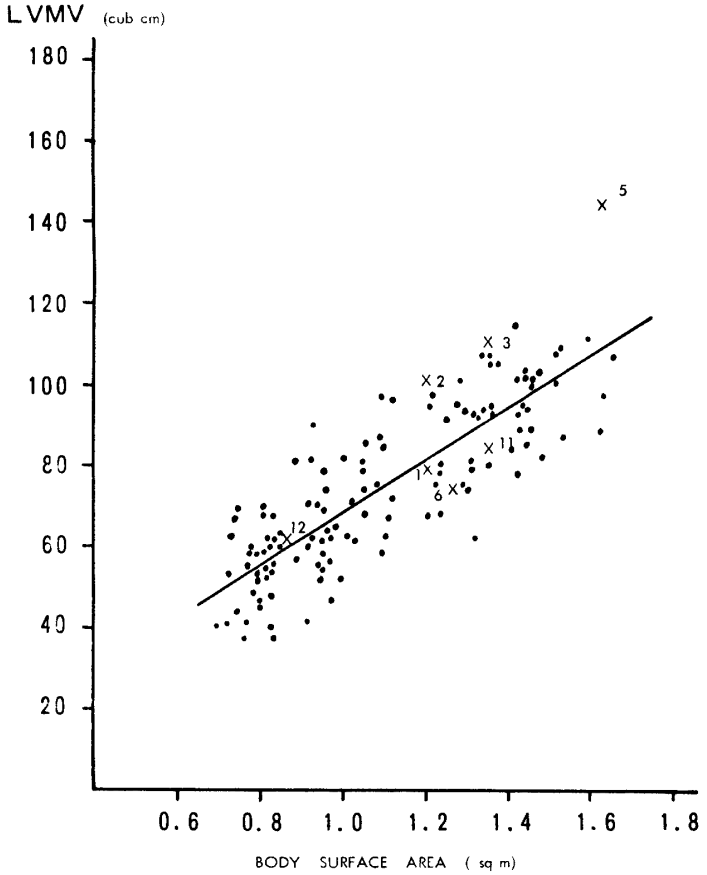

Fig. 3. LVMV plotted against body surface area in hypertensive (×) and normotensive (●)girls.

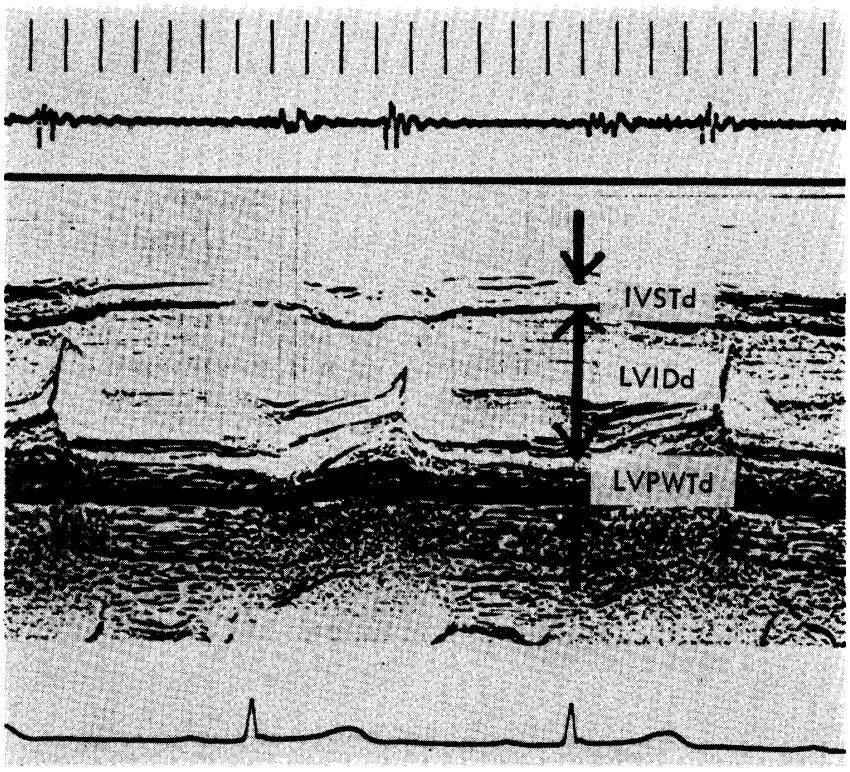

Fig. 4. Echocardiogram with Case 5, 14-year-old girl with "borderline" hypertension (132/80). LVMV is markedly increased (145.8 ccm).

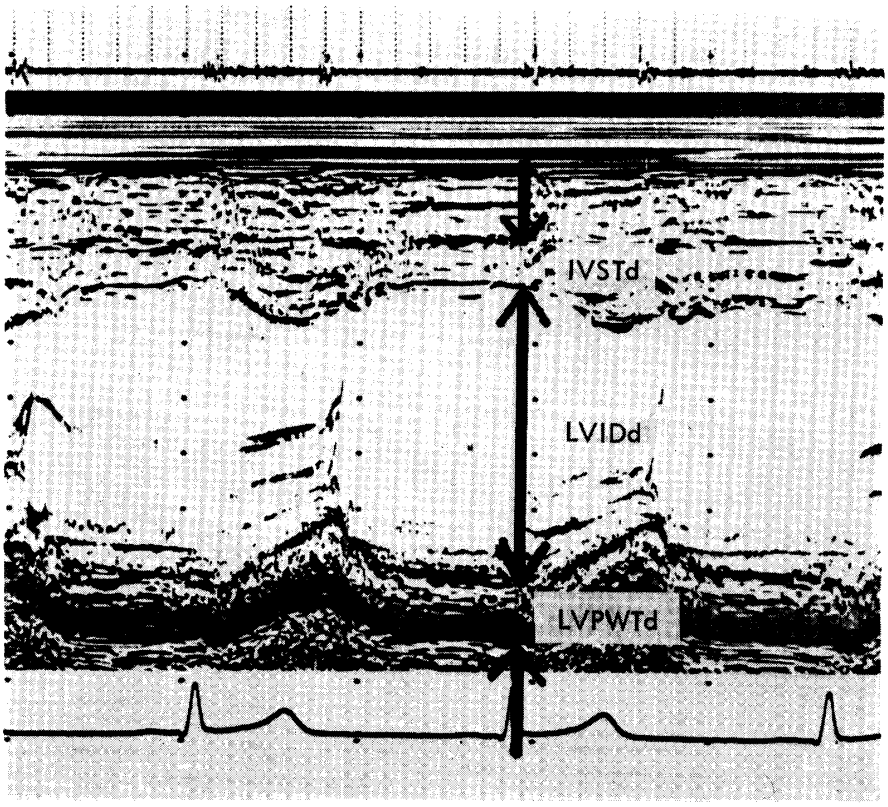

Fig. 5. Echocardiogram of Case 9, 14-year-old boy with moderate hypertension (166/100). LVMV is markedly increased (163.2 ccm).

with renovascular disease. The duration of his hypertensive state was about 12 months. His LVMV of 163.2 ccm indicated that he had left ventricular hypertrophy.

4. Relationship between family history and the values of blood pressure, serum cholesterol and LVMV(Tables III and IV)

There was no significant difference in these values between children with a family history of apoplexy aud those without.

TABLE III. *Blood Pressure of Children with or without a Family History of Apoplexy (Mean±S. D.)*

	Age(yrs)	Sex	Family history of apoplexy (+)	(−)
			mmHg	mmHg
Systolic	6– 7	Male	91.5± 6.7	91.7±6.8
		Female	89.5± 5.5	95.1±8.7
	9–10	Male	105.8± 6.4	103.4±8.9
		Female	108.4±13.7	104.7±9.4
	12–15	Male	110.1±12.8	108.1±9.1
		Female	108.1± 8.6	111.9±8.1
Diastolic	6– 7	Male	51.2± 6.1	52.4±7.8
		Female	48.7± 7.9	54.1±9.8
	9–10	Male	62.6± 5.6	61.1±7.5
		Female	62.2± 9.8	60.4±8.3
	12–15	Male	66.4± 9.0	62.7±6.6
		Female	64.6± 6.2	64.0±6.1

TABLE IV. *Serum Cholesterol Levels and LVMV of Children with or without a Family History of Apoplexy (Mean±S. D.)*

	Age(yrs)	Sex	Family history of apoplexy (+)	(−)
			mg/dl	mg/dl
Cholesterol	6– 7	Male	141.2±19.1	151.7±25.1
		Female	144.1±17.1	155.7±22.1
	9–10	Male	147.6±17.2	156.9±16.8
		Female	143.6±14.1	144.7±19.7
	12–15	Male	152.9±45.8	134.8±21.6
		Female	138.9±22.9	145.3±21.4
			cub. cm	cub. cm
LVMV	6– 7	Male	62.2±10.5	60.0±10.4
		Female	56.9±11.8	54.9± 8.5
	9–10	Male	74.4±12.3	76.0±14.0
		Female	75.9±12.1	72.2±14.6
	12–15	Male	112.5±22.5	107.0±17.4
		Female	97.4± 8.5	93.4±15.7

DISCUSSION

1. Left Ventricular Hypertrophy in Early Hypertension

In longstanding and established hypertension, left ventricular hypertrophy is a well known finding which can be demonstrated by electrocardiography or echocardiography (8, 9). On the other hand, recent progress in studies of spontaneously hypertensive rats have helped to clarify the concept that left ventricular hypertrophy already begins before or immediately after the development of hypertension.

Sen *et al.* (1) reported that the early increase in ventricular weight was evident before "hypertensive" pressure levels were recorded in spontaneously hypertensive rats. Recently a similar observation was made by Ohshima *et al.* (2) on early hypertrophy of heart muscle in spontaneously hypertensive rats. The *in vitro* incorporation of ^{14}C-leucine into heart tissue was already increased in the pre-hypertensive stage.

These observations in experiments on animals suggest that analogous changes may be observed in human beings before or immediately after the development of hypertension. To support the hypothesis, LVMV was compared between children with and without risk factor for hypertension (based on family history of apoplexy as discussed later). Further, LVMV of hypertensive children was studied to demonstrate whether or not ventricular hypertrophy existed immediately after the development of "borderline" hypertension.

Increased LVMV was not observed in children with risk factor for hypertension before its development. However, enlargement of LVMV was demonstrated in a 14-year-old girl with "borderline" hypertension (Case No.5). In this case, there was a family history of hypertension. Her LVMV was 145.8 ccm (normal 93.5 ± 12.0ccm) in spite of a "borderline" hypertension (132/80).

This finding strongly suggests that the ventricular hypertrophy can also occur in human beings immediately after the development of hypertension or in pre-hypertensive states as shown in animal experiments (1, 2).

To generalize the concept of early development of left ventricular hypertrophy in pre-hypertensive states, we are now planning to follow up this patient and to carry on related studies in similar occurrences.

An enlarged LVMV during childhood could be considered to be a risk factor for hypertension and its early detection would be important for the prevention of hypertension.

Although non-obstructive cardiomyopathy reveals a left ventricular hypertrophy similar to that seen in our patient, disorder usually shows a familial tendency and is not accompanied with hypertension (10, 11). On the contrary, our patient had hypertension and a negative family history for the disorders. Therefore, non-obstructive cardiomyopahy was excluded.

2. *Relationship between Family History of Hypertension and the Values of Blood Pressure, Serum Cholesterol and LVMV*

Family history of hypertension is obviously one of the risk factors for hypertension (12), but the history itself is not always reliable, as the criteria of hypertension are variable and not all family members have their blood pressure taken. On the contrary, attack of apoplexy is so dramatic that the family history of apoplexy is more reliable than that of hypertension. In addition, hypertension is the most frequent etiology of apoplexy in Japan (13).

For the reasons mentioned above, the family history of apoplexy was chosen in our study as the most reliable risk factor for hypertension.

In the hope of detecting early pathophysiologic changes associated with hypertension, we compared values of left ventricular muscle volume, blood pressure, and serum cholesterol between groups of children with and without risk factor of hypertension, that is, family history of apoplexy.

The results revealed no significant differences between these two groups, but such a finding does not necessarily mean that the children with a family history of hypertension will not have a hypertension later on in life. Changes accompanying hypertension may not yet be apparent at the time of investigation of these children.

As the period of school age may be a premanifestive phase of hypertension, we are planning a follow-up of the study population, and an investigation of the higher age groups.

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