FOREARM VASCULAR RESISTANCE IN THE UPPER AND
LOWER QUINTILES OF BLOOD PRESSURE IN ADOLESCENT BOYS:
The Muscatine Study

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Running Title: Forearm Vascular Resistance in Children

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Abstract:

Nineteen 16 year old white boys whose systolic blood pressures were in the upper ($r = 9$) and lowest ($r = 10$) quintile of the distribution in two school surveys in 1975 and 1977 were selected. In 1979 forearm blood flow, blood pressure and heart rate were measured at rest, and during peak reactive hyperemia. Minimal forearm vascular resistance during peak reactive hyperemia was used to assess the structural contribution to vascular resistance. At rest the high quintile group again had significantly higher blood pressures than the low quintile group but their forearm vascular resistance was not significantly different. The high quintile group showed significantly higher minimal forearm vascular resistance at peak reactive hyperemia. The latter observation suggests that there is a difference in the structural contribution to forearm vascular resistance in adolescents with blood pressure in the upper versus lower quintile of the distribution.

Speculation:

The limitation of forearm vasodilation during peak reactive hyperemia in adolescents with blood pressures in upper quintile compared to the lowest quintile of the blood distribution is similar to the observed difference between adult hypertensives and normotensives. This suggests that those in the upper quintile may be the future hypertensive adults.

In adults, borderline hypertension is characterized by an abnormal relationship between cardiac output and peripheral resistance resulting in elevated blood pressure.^{8-9,12} Structural changes in the systemic resistance vessels have been demonstrated both in experimental animal models and adult human hypertensive patients.^{6-7,14} In hypertensive adolescents, marked hemodynamic heterogeneity has been observed with various degrees of increased cardiac output and peripheral vascular resistance responsible for elevated blood pressure.^{3,5}

In young children the level of blood pressure which may be termed "hypertension" is unclear. In a longitudinal study we have identified school children in Muscatine, Iowa whose blood pressures are repeatedly in the highest, intermediate or lowest range for their age.¹ In this population Schieken et al.,¹³ utilizing echocardiographic measurements, have demonstrated that cardiac output and total systemic vascular resistance is heterogeneous in these three groups of children. Those in the upper quintile of blood pressure had significantly thicker interventricular septa and left ventricular posterior walls than those in the middle or lower quintile. Although resting vascular resistance was similar in these three groups, studies in adults indicate that abnormalities in vascular control and the structural component of vascular resistance may exist even with normal resting vascular resistance.¹⁷

In the study presented herein age, sex, and anthropometrically matched children whose blood pressures remained consistently in the highest quintile and lowest quintile of blood pressure were compared with respect to their forearm blood flow and resistances at rest and during peak reactive hyperemia. Minimal vascular resistance during peak reactive hyperemia after 10 minutes of arterial occlusion is thought to indicate the structural contribution to vascular resistance.^{2,6,7,17} The study showed similar resting vascular resistance in both groups. However, vasodilator capacity was less in the high blood pressure group suggesting that there is a difference in the structural contribution to vascular resistance between the high and low blood pressure groups.

Material and Methods

The study was undertaken in nineteen white male subjects in 1979. Nine of these were selected because they had systolic blood pressures greater than or equal to the 80th percentile for age both in a 1975 and a 1977 survey of the school population of Muscatine, Iowa.¹ These nine are referred to as the high blood pressure group. Ten were selected because they had systolic pressures equal to or less than the 20th percentile in both survey years. The latter ten are referred to as the low blood pressure group. The individuals in the high group were selected to resemble an individual in the low group in age, height and weight, at the time of their 1977 examination in the Muscatine schools. Table 1 shows the mean and standard deviation

of the measurements obtained at the time of forearm blood flow measurements in 1979. Because of differential growth rates, the pairs of subjects were not as closely matched in body size as they were at the time of the 1977 measurements. However, as groups, their ages, heights, and weights were not significantly different.

The subjects were asked to participate in this study after it was approved by the Human Study Committee of the University of Iowa. Written consent was obtained from the students and their parents.

The examinations were conducted in a trailer whose temperature was kept ambient at 22°C. At the outset, the subjects' height, weight and forearm circumference were measured. A seated casual blood pressure in the right arm was measured in the same fashion as in the Muscatine school survey.¹

All other measurements were obtained with the subjects in the a supine position. Forearm blood flow was measured in the right arm using a mercury-in-silastic strain gauge plethysmograph and venous occlusion.¹⁴ During measurements of forearm blood flow, circulation to the hand was arrested by inflating a cuff around the wrist to suprasystolic pressure.⁴ Initially four flows were recorded every 10 seconds, and an average value calculated, while blood pressure was measured in the left arm with a Roche Arteriosonde (model 1216) blood pressure monitor.

In seventeen other children with congenital heart disease, ages 6 through 17 years, who underwent catheterization for diagnostic purposes, we found the correlation of intraaortic arch pressures with Arteriosonde pressures to be $r = 0.88$ for systolic and $r = 0.89$ for diastolic pressures.

Forearm vascular resistance was calculated by dividing mean arterial blood pressure (diastolic pressure plus 1/3 of pulse pressure) by forearm blood flow (ml/minute/100 ml forearm volume). Heart rates were measured from electrocardiographic records obtained over periods of 6 seconds at paper speeds of 25 mm/second.

Minimal vascular resistance was assessed in the two groups by inflating the cuff on the upper arm to suprasystolic pressure for 10 minutes to occlude arterial flow. After release of arterial occlusion, forearm blood flow and blood pressures were measured after 5 seconds and every 10 seconds thereafter for 3 minutes. Blood pressures were measured at approximately 30 second intervals after the release of the arterial occluding cuff. The peak blood flow recorded after release of arterial occlusion was used to calculate the minimum forearm vascular resistance.

The differences between the two groups were analyzed by unpaired student's t-tests.

RESULTS

Table 1 presents mean values for age, height, weight, forearm circumference, heart rate, seated and recumbent blood pressure and calculated forearm vascular resistance of the low and high blood pressure groups. There were no significant differences between the groups in age, height, weight, forearm circumference and heart rate. Both the seated and recumbent systolic blood pressures in the two groups were significantly different, while the diastolic pressures were not. The calculated mean blood pressure of the two groups was significantly different. The forearm vascular resistance was not different at rest in the two groups.

A representative recording of forearm blood flow and blood pressure during reactive hyperemia is presented in Figure 1. Following 10 minutes of arterial occlusion, blood flow was increased approximately ten-fold and then declined toward control levels. Blood pressure and heart rate did not change significantly during reactive hyperemia. Table 2 shows the blood pressure, forearm blood flow and vascular resistance at peak reactive hyperemia in both groups. Systolic and mean blood pressures continued to be significantly different between groups. Maximal forearm blood flow tended to be lower in the high blood pressure group but did not differ significantly. However, forearm vascular resistance at peak reactive hyperemia was significantly higher ($p < 0.05$) in the high blood pressure group (3.2 ± 0.9 mm Hg/minute/100 ml) than in the low blood pressure group (2.4 ± 0.6 mm Hg/minute/100 ml).

Discussion

Although blood flow, pressure and resistance have been widely studied in normotensive and borderline hypertensive adults^{8-10,12,15-17,20} only limited studies have been performed in adolescents.^{3,5,8} The limited number of hemodynamic studies in young children and adolescents is perhaps related to ethical considerations associated with invasive studies in the pediatric age group.

The Muscatine longitudinal study of casual blood pressure levels of school age children has enabled identification of those whose blood pressures are consistently low or high in the blood pressure distribution.¹ The present study was undertaken to examine noninvasively some of the mechanisms responsible for the differences in blood pressure in the highest and lowest quintiles in this young population, and specifically to compare forearm vascular resistance in the two groups.

The group differences in seated casual blood pressure which had been detected during the initial Muscatine school surveys were maintained at the time of this study both in the seated and recumbent positions. Forearm blood flow in the highest quintile group tended to be higher than that in the lowest quintile group.

Despite the higher arterial or distending pressure in the high blood pressure group, forearm resistance was similar in the two groups. Thus, the high blood pressure group did not decrease resistance in the face of a higher distending pressure. This suggests that these subjects have abnormalities of control of forearm vascular resistance. These abnormalities could involve neurogenic, humoral, autoregulatory, or structural vascular alterations.

We studied these subjects of forearm hemodynamics at peak reactive hyperemia, when an index of the structural component of vascular resistance can be measured. Takeshita and Mark¹⁷ have shown that hyperemia is maximal after 10 minutes of arterial occlusion and that it is reproducible with an average difference between measurements in the same individual of 6%. Peak reactive hyperemia is associated with blood flows that are greater than or equal to those during exercise, heating or intra-arterial administration of vasodilator agents such as acetylcholine, histamine, adenosine triphosphate or sodium nitrate.^{2,4,17,19} The validity of measuring high flow rates by plethysmographic methods has been studied by Folkow⁶ and Conway.² They noted that if the veins are emptied or collapsed before occluding the cuff, as was true in this study, the linear portion of the recording occurs before the increase in venous pressure which could interfere with the measurement. In addition the observations of Takeshita and Mark¹⁷ and Folkow et al.⁶ indicate that a transient reduction in perfusion pressure does not account for higher values of minimal vascular resistance in borderline or established hypertensives.

All these observations indicate that the minimal vascular resistance measured at peak reactive hyperemia is an index of the structural component of vascular resistance.

In this study, at peak reactive hyperemia forearm vascular resistance was significantly greater in the high blood pressure group as compared to the low blood pressure group. Thus, the high blood pressure group appears to have a limitation of vasodilator capacity of forearm resistance vessels. This suggests that structural changes are present at an early age in those whose blood pressures remain consistently in the upper quintile of the blood pressure distribution. Structural vascular changes might involve vascular smooth muscle hypertrophy with increased wall to lumen ratio,^{6,7,14} water logging,¹⁸ a decreased number of resistance vessels as shown in the spontaneously hypertensive rat,¹¹ or a decrease in the size of vessels without vascular hypertrophy.¹⁴ Since we evaluated vasodilator capacity by a physiological technique rather than by morphologic methods, we cannot define the specific nature of the vascular abnormality. Despite the physiological evidence of structural changes in forearm resistance vessels, resting forearm vascular resistance was not significantly increased in the high quintile group. Nevertheless, such mild structural vascular changes might produce significant hemodynamic consequences by augmenting the response to vasoconstrictor stimuli or by limiting vasodilation.^{7,14} This study did not examine those with blood pressures in the middle range. Thus, it is possible that the response in the lowest quintile is exaggerated.

However, the limitations of forearm vasodilation at peak reactive hyperemia has also been observed in adult hypertensives, suggesting that the upper quintile group has a similar limitation.

It is important to stress that the two groups of children in this study were selected on the basis of two casual seated systolic blood pressure measurements taken approximately two years apart. The group in the high quintile of blood pressure did not have pressure levels which are usually considered as hypertensive. The mean blood pressures of the high quintile group were 124 mm Hg systolic and 76 mm Hg diastolic in the recumbent position after rest. On examination at the time of this study the students in the high and low blood pressure groups were again observed to have levels of pressure which were different from each other in the seated and recumbent positions. This study indicates that repeated measurements of casual blood pressure can identify groups of children not only with different blood pressures but also with different structural contribution to vascular resistance. The observations that blood pressure level maintains a significant degree of peer rank order throughout childhood,¹ and that children in the upper part of the distribution may have a limitation of vasodilator capacity similar to that observed in adult hypertensives,¹⁷ suggest that children with blood pressures in the upper part of the distribution for their age may be predisposed to the development of hypertension as adults.

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Table 1: Mean Values For Initial Readings
(Mean $\pm$ Standard Deviation)

		Lowest Quintile Group	Highest Quintile Group	p
Number		10	9	
Age (yrs)		16.9 $\pm$ 1.3	16.6 $\pm$ 0.7	.55
Height (cm)		169.9 $\pm$ 2.4	168.3 $\pm$ 2.5	.17
Weight (kg)		68.8 $\pm$ 6.9	69.4 $\pm$ 7.1	.87
Arm Circumference (cm)		27.3 $\pm$ 1.5	26.9 $\pm$ 1.5	.06
Heart Rate (beats/min)		66.1 $\pm$ 8.8	67.1 $\pm$ 12.5	.84
Resting Forearm Blood Flow (ml/min/100 ml)		3.75 $\pm$ 1.12	5.21 $\pm$ 3.13	.18
Resting Forearm Vascular Resistance (mm Hg/ml/min/100 ml)		23.0 $\pm$ 7.4	22.7 $\pm$ 11.3	.94
Systolic Blood Pressure (mm Hg)	seated	121.2 $\pm$ 9.6	142.7 $\pm$ 13.1	.001
	recumbent	103.5 $\pm$ 11.9	123.4 $\pm$ 11.6	.002
Diastolic Blood Pressure (mm Hg)	seated	78.8 $\pm$ 10.6	83.8 $\pm$ 17.2	.45
	recumbent	67.3 $\pm$ 9.6	76.0 $\pm$ 8.5	.05
Mean Blood Pressure (mm Hg)	seated	92.9 $\pm$ 9.9	103.2 $\pm$ 12.3	.05
	recumbent	79.4 $\pm$ 9.5	91.8 $\pm$ 9.0	.01

Figure 1: Forearm blood flows and blood pressures recorded before arterial occlusion and during peak reactive hyperemia.

Table 2: Blood Pressure, Forearm Blood Flow
and Resistance at Peak Reactive Hyperemia
(Mean $\pm$ Standard Deviation)

	Lowest Quintile Group n=10	Highest Quintile Group n=9	p
Systolic Blood Pressure (mm Hg)	107.2 $\pm$ 12.2	123.4 $\pm$ 7.3	.004
Diastolic Blood Pressure (mm Hg)	73.3 $\pm$ 10.5	79.4 $\pm$ 7.2	.18
Mean Blood Pressure (mm Hg)	84.6 $\pm$ 10.4	94.1 $\pm$ 6.5	.04
Maximal Forearm Blood Flow (ml/min) (100 ml)	47.2 $\pm$ 14.9	41.4 $\pm$ 14.4	.40
Minimum Forearm Vascular Resistance (mm Hg) (ml/min/100 ml)	2.4 $\pm$ 0.6	3.2 $\pm$ 0.9	.03

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