Studies on innocent praecordial vibratory murmurs in children¹

III: Follow-up study of children with an innocent praecordial vibratory murmur

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A group of 40 children, originally examined for an innocent praecordial vibratory murmur were reinvestigated after a mean follow-up period of 6.9 years (range 3.2 to 11.5).

All were subjected to a non-invasive cardiological examination, comprised of anamnesis, physical examination, electrocardiogram, phonocardiogram with pulsation tracings, and x-ray examination of the chest.

From simultaneous recording of the electrocardiogram, phonocardiogram, and carotid artery tracing in supine position at rest, left ventricular ejection time and pre-ejection period were calculated.

In one of the 40 subjects re-examined, suspicion was aroused concerning the existence of a cardiac malformation. At cardiac catheterization a minimal haemodynamic abnormality was found with a doubtful relation to the original praecordial murmur.

A positive statistical correlation was found between pubertal development on disappearance of the murmur.

Subjects in whom the murmur had disappeared and subjects in whom a grade 2 praecordial murmur was still present at follow-up were individually matched on the basis of body height with subjects from the group of 85 normal controls investigated previously. In both sets of twin groups left ventricular ejection time and pre-ejection period were compared to standard adult values.

No difference in left ventricular ejection time and pre-ejection period was found between the groups of children in whom the murmur had disappeared and their matched controls. The children still presenting a grade 2 murmur at follow-up, however, had lower pre-ejection periods for equal heart rate than their matched normal controls without a murmur. This finding confirms the results of a former study on children with an innocent praecordial vibratory murmur (de Monchy, van der Hoeven, and Beneken, 1973).

The innocent praecordial vibratory murmur is found only in children (Marienfeld *et al.*, 1962). Here it constitutes the majority of innocent murmurs (Paulin and Mannheimer, 1957). Though Marienfeld proved its ultimate disappearance, no information has been published on the relation between puberty and the disappearance of the murmur. Therefore, a follow-up study was undertaken in order to investigate this possible relation. A follow-up investigation in a group of these children could also throw some light on the question of the con-

sistency of the original diagnosis and its possible relation to subclinical forms of rheumatic heart disease (Luisada, 1955) or congenital heart disease (Nadas, 1963). Finally, a previous study having demonstrated a significantly shorter pre-ejection period in children with an innocent praecordial vibratory murmur, interest was aroused in measuring systolic time intervals in subjects who had previously shown one but in whom the murmur had disappeared.

Subjects and methods

Sixty-eight subjects were chosen from the files of the Wilhelmina Children's Hospital, Utrecht, on the criteria

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for innocent praecordial vibratory murmurs, as mentioned in a previous article on children with an innocent praecordial vibratory murmur (part II of this series: de Monchy *et al.*, 1973). All children had a grade 2 murmur at initial examination. The original examination took place between 1960 and 1968, and was performed by one of the authors (de Monchy).

Most of the children were followed for several years, with repeated phonocardiograms confirming the diagnosis.

Of these 68 subjects, 64 could be traced. They (and/or their parents) were approached by letter explaining the reasons for the reinvestigation and soliciting their voluntary co-operation. Fifty-three answers were received (82% of the subjects approached), 6 of which were negative. Of the 47 subjects willing to co-operate, 6 did not appear at the agreed time and failed to answer a repeat summons. Of the 41 subjects examined, one had to be dropped from the study owing to a technical breakdown during recording.

All children were subjected to the following routine.

- 1) Interval anamnesis for complaints, possibly related to the cardiovascular system.
- 2) Physical examination. Presence or absence of a cardiac murmur was noted. If present, the loudness of the murmur was assessed according to the grading of Freeman and Levine (1933), and the presence or absence of a vibratory quality was noted. Signs of puberty were assessed according to the method of Tanner (1962).
- 3) Electrocardiogram and phonocardiogram were recorded in the supine position, at rest, paper speed 50 mm/sec.
- 4) Systolic intervals were measured according to the method of Weissler, Harris, and Schoenfeld (1969), paper speed 100 mm/sec, in the same way as described earlier (part I of this series: van der Hoeven, de Monchy and Beneken, 1973).

Follow-up interval

Mean age at first examination was 5.7 years, mean follow-up period 6.9 years, range 3.2 to 11.5 years. Age of children re-examined ranged from 5.5 to 20.3 years.

The subjects were classified according to the loudness of the murmur at follow-up examination into 3 groups: grade 2, grade 1, and grade 0 (no murmur detectable).

In order to compare systolic time intervals, the children with a grade 2 murmur and those without a murmur were matched individually with subjects from the group of 85 normals, investigated previously (van der Hoeven *et al.*, 1973), on the basis of nearest body height in the same manner as in the previous study on children with an innocent praecordial vibratory murmur (de Monchy *et al.*, 1973). This parameter was chosen because biological age is more closely related to height than to chronological age (Tanner, 1962). Body weight is too easily influenced by incidental factors to be of value as a basis of comparison. In the subjects above the age of 15 years, sex was also taken into account, as in adults male and female values for systolic time intervals are slightly different (Kesteloot and Willems, 1967;

Golde and Burstin, 1970). In all but one instance, sex and height-matched controls could be found.

When chosen according to nearest body height, the groups of matched controls show nearly identical mean values for age and body weight, but heart rates differ considerably. This finding will be discussed later. The statistical significance of the various parameters was tested by Student's *t* test and χ^2 test, according to the methods of Snedecor (1967).

Results

Consistency of diagnosis

In one subject re-examination revealed a delayed upstroke time on the femoral artery tracing. In addition, *x*-ray examination of the chest showed a slight notch in the descending aorta, possibly due to coarctation. The child was referred to a cardiac diagnostic centre for further diagnostic studies.

These demonstrated a normal aorta and the presence of an abnormal pulmonary venous return to the right subclavian vein with a shunt volume too small for calculation from oxygen-saturation values.

TABLE 1 *Relation between pubertal development and disappearance of the innocent praecordial vibratory murmur at follow-up examination*

Grades of puberty	No.	Mean age	Murmur		
			Grade 2	Grade 1	Grade 0
{0	16	9.1	5	9	2
{1	3	12.1	0	2	1
{2	4	12.7	2	2	0
{3	7	13.7	3	3	1
{4	2	16.2	0	1	1
{5	7	16.8	0	2	5

No., number of subjects; grade 0, no murmur detectable.

TABLE 2 *Relation between pubertal development and disappearance of the innocent praecordial vibratory murmur at follow-up examination*

Grades of puberty	Grade 2	Grade 1	Grade 0	Total
0-1	5	11	3	19
2-3	5	5	1	11
4-5	0	3	6	9
Total	10	19	10	39

Note: When tested with the χ^2 test the null hypothesis is rejected at a *P* value of <0.02 . Therefore a statistically significant relation exists between the development of puberty and the disappearance of the murmur.

TABLE 3 Values for body height, age, body weight, heart rate, and systolic time intervals of children without a murmur at follow-up examination and their matched controls from a group of normal individuals, chosen on the basis of nearest body height; corresponding numbers are matched

Subject No.	Sex	Height (cm)	Age (yr)	Weight (kg)	Heart rate	LV ejection time (msec)	Pre-ejection period (msec)
<i>Grade 0: Murmurs at follow-up</i>							
1	F	140	12.0	50	69	326	98
2	M	172	16.7	54.5	57	303	92
3	M	151	12.4	37	64	309	111
4	M	176	15.1	65	51	303	110
5	M	149	17.3	32	51	308	103
6	M	184	16.7	68	59	305	125
7	F	170	20.3	62	74	299	79
8	F	141	11.1	27	85	265	99
9	M	170	13.0	45	58	288	120
10	M	173	17.1	66.5	46	323	123
Mean	3 F	162.6	15.17	50.70	61.4	303	106
SEM	7 M					5.4	4.6
<i>Controls</i>							
1	M	142	12.0	54	89	240	111
2	M	167	21.0	57	76	275	101
3	F	149	11.5	35	82	300	88
4	M	177	19.0	67	69	277	102
5	F	149	15.7	37	84	235	101
6	M	185	18.9	69	49	292	105
7	F	174	18.7	59	89	295	81
8	F	141	10.1	36	83	280	83
9	M	170	13.4	45	91	247	77
10	M	176	20.3	72	63	284	95
Mean	4 F	163.0	16.06	53.12	77.5	272.5	94.4
SEM	6 M					7.4	3.6

SEM, standard error of mean.

Relation between disappearance of murmur and puberty

In Table 1 the subjects are classified according to pubertal development and classification of loudness of the murmur at auscultation. When pubertal development is assessed in 3 stages, the relation between the disappearance of the murmur and pubertal development is statistically significant (Table 2).

Systolic time intervals

All subjects with a grade 2 murmur and those without a murmur at follow-up examination were individually matched with normal controls. The results of the measurements are given in Tables 3 and 4. Fig. 1 presents mean values for left ventricular ejection time and pre-ejection period in each group with normal adult values according to Weissler *et al.* (1969) added as a reference base for heart rate correction.

Discussion

Consistency of diagnosis

In only one of the subjects re-examined was a suspicion of organic heart disease aroused. At cardiac catheterization, an abnormal pulmonary vein was found with a shunt volume too small for calculation from oxygen saturation values. The relation between this minimal abnormality and the presence of a detectable praecordial murmur can be considered doubtful. In conclusion, this study has given no indication of significant occurrence of heart disease in the group of children re-examined.

Relation between disappearance of murmur and puberty

The relation between pubertal development and the disappearance of the murmur (Tables 1 and 2) might also be a result of age, as pubertal development is age dependent. In order to separate these two influ-

TABLE 4 Values for body height, age, body weight, heart rate, and systolic time intervals of children with a grade 2 murmur at follow-up examination and their matched controls from a group of normal individuals, chosen on the basis of nearest body height; corresponding numbers are matched

Subject No.	Sex	Height (cm)	Age (yr)	Weight (kg)	Heart rate	LV ejection time (msec)	Pre-ejection period (msec)
<i>Grade 2: murmurs at follow-up</i>							
1	M	120	6.8	21	74	278	80
2	F	112	6.3	18	81	283	68
3	M	155	12.7	36	76	286	60
4	M	150	11.1	41	68	302	85
5	F	166	13.2	54.5	72	318	82
6	M	165	14.0	46	66	317	79
7	F	157	15.0	54.5	66	319	100
8	F	112	5.5	21.5	82	288	92
9	F	145	11.6	47.0	65	308	91
10	F	155	13.2	46	75	295	97
Mean		143.7	10.94	38.55	72.5	299.4	83.4
SEM						4.9	3.9
<i>Controls</i>							
1	M	122	6.0	21.4	70	296	75
2	M	114	6.3	19.2	70	296	91
3	M	153	12.7	41.5	89	272	80
4	M	148	11.3	42.2	86	262	84
5	F	167	16.0	50.0	72	282	97
6	F	161	15.8	52	80	272	110
7	F	151	14.6	57	104	247	90
8	F	114	5.5	21.7	98	281	82
9	F	144	10.5	53	75	280	122
10	F	149	15.7	37	84	235	101
Mean		142.3	11.44	39.50	82.8	272.3	93.2
SEM						6.0	4.6

SEM, standard error of mean.

ences statistically, a much larger number of subjects would have been necessary.

It can only be stated that at the beginning of puberty, 16 of the 19 subjects still had a detectable praecordial murmur, whereas this was only the case in 3 of the 9 subjects who showed advanced or completed maturation.

Systolic time intervals

The two sets of groups (with and without a murmur, each with its group of matched controls, Tables 3 and 4) were comparable in all respects except heart rate. The subjects from the follow-up study had consistently lower heart rates than the normal controls. This difference was significant in all groups (Fig. 2). An explanation for this difference may lie in the fact that the controls were investigated in the hospital. The follow-up group, however, was investigated in the laboratory of the Institute of Medical Physics, in a very different setting without the atmosphere of the hospital. It may be presumed

that these surroundings, combined with the element of voluntary co-operation granted by the subjects and/or their parents, created a much more relaxed atmosphere in which the children attained or nearly attained true basic heart rates at rest. Though this may explain the reason for the difference in heart rates, the fact remains that valid statistical calculations in respect to pre-ejection periods and left ventricular ejection times in the corresponding groups become impossible for this reason.

All that can be done is to present the figures of the four groups together with the standard adult values, as given by Weissler, in order to approximate the slope of the correction for heart rate (Fig. 1).

Left ventricular ejection time (Fig. 1A) No murmur at follow-up examination. It seems that with advanced pubertal development children have significantly shorter left ventricular ejection times for heart rate than adults. This seems the case for the follow-up group as well as for the group of matched

FIG. 1 Mean values for left ventricular ejection time (A and B) and pre-ejection period (C and D) in children presenting without a murmur at follow-up investigation (A and C) and with a grade 2 murmur (B and D). Mean value of each group is compared to the corresponding mean value of a group of individually matched normal controls without a murmur.

Normal adult values according to Weissler are added as a reference base for heart rate correction.

normal controls. This phenomenon was also apparent in the age group 15 to 20 years of the first study in this series (normal children). No explanation can be given on the basis of the available facts.

Left ventricular ejection time (Fig. 1B) Grade 2 murmur at follow-up examination. In these groups with lower age range the follow-up group as well as the group of matched controls approximates adult values.

Pre-ejection period (Fig. 1C) No murmur at follow-up examination. The groups do not differ from each other if the heart rate is corrected according to the slope of adult values.

Pre-ejection period (Fig. 1D) Grade 2 murmur at follow-up examination. The group of matched controls has values slightly below adult values, the same as the whole group of normals from which this

FIG. 2 Heart rates versus age at rest in supine position of children investigated during their stay in hospital (matched controls) or investigated on the basis of voluntary co-operation in a laboratory setting (murmurs follow-up).

sample was chosen. The group of children with a murmur, however, show values considerably shorter than would have been expected on the basis of heart rates. This confirms the conclusions from the second study in which a different group of children with an innocent praecordial vibratory murmur also showed significantly shorter pre-ejection period than children without a murmur.

Conclusions

Children with an innocent praecordial vibratory murmur have shorter pre-ejection period values than children without a murmur. The left ventricular ejection times do not differ significantly.

At puberty the murmur disappears, and together with the disappearance of the murmur the pre-ejection period reverts to normal.

The diagnosis of innocent praecordial vibratory murmur in children can be made with reasonable confidence. Calculation of pre-ejection period can be of value in sustaining the diagnosis.

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