Dermatoglyphics in Congenital Heart Disease

By Milton Alter, M.D., Ph.D., and Robert Schultenberg, M.D.

SUMMARY

Dermatoglyphics form in utero during early gestation and may be influenced by genetic or environmental factors operating at that time. Since cardiac embryogenesis also occurs during early gestation, an analysis of dermatoglyphics in congenital heart disease (CHD) might reveal some types which are associated with aberrant dermatoglyphics.

Ten dermatoglyphic traits were analyzed in 225 individuals with CHD proved, in most instances, by extensive radiologic studies and at surgery. These traits were compared with dermatoglyphics in 200 normal control subjects. The analysis revealed that the atd angle was significantly increased in CHD. Except for endocardial fibroelastosis and atrioventricular canal, all subtypes of CHD had a wider atd angle than controls. In ventricular septal defect, patent ductus arteriosus, tetralogy of Fallot, and multiple cardiac defects, the increase was statistically significant. The present study confirms previous reports that the atd angle may be increased in CHD.

Additional Indexing Words:

atd angle  Mongolism  Axial triradius  Cardiac embryology

Most congenital cardiovascular anomalies have their genesis early in gestation during embryogenesis of the individual organs or organ systems. In the majority of cases of congenital heart disease (CHD), no specific etiologic basis has been established. However, a number of such anomalies are clearly of genetic origin resulting either from single gene disorders or gross chromosomal aberrations. Specific environmental influences have also been implicated as causative factors. McKusick stated that polygenic inheritance is an important genetic mechanism in the common forms of congenital heart disease. Other authors have speculated that a large percentage of cardiovascular anomalies are the result of interplay between both genetic and environmental factors with the relative importance of each factor varying according to the specific lesion involved.

Dermatoglyphic configurations formed by the epidermal ridges on fingers, palms, and soles begin to develop during the sixth to seventh week of fetal life. Development is completed by the fourth month of gestation and thereafter the patterns remain the same. There is wide agreement that the mechanism of inheritance of many dermatoglyphic features also conforms to a polygenic system with each gene contributing a small additive effect. Examples of these dermatoglyphic traits are the transversality of the ridges on the palm, the a-b ridge count, and the atd angle. Other features such as the calcar patterns appear to be influenced by a single gene. Information as to the loci that influence dermatoglyphics is still speculative, but various reports have appeared that implicate chromosome 21 in the determination of finger ridge count and the position of the axial triradius. Other chromosomal loci of genes influencing dermatoglyphics include the X chromosome and chromosome 18.
The literature contains abundant evidence concerning the value of dermatoglyphics in the diagnosis of various chromosomal disorders,17-19 in diseases transmitted as autosomal dominant or recessive traits,20-22 and in diseases in which genetic transmission is uncertain.23, 24 More recently, it has been reported that exogenous environmental agents, such as rubella, may also alter dermatoglyphics and be useful in providing evidence of such an exposure.25-27

It has been noted that individuals with various chromosomal aberrations such as trisomy G, D, and E have a high frequency of various cardiovascular malformations in association with other organ system involvement.28-30 They also have aberrant dermatoglyphics. Those having single gene disorders with cardiovascular involvement almost all have extracardiac malformations including unusual dermatoglyphics.21, 22 In view of the apparent association between cardiac malformations and aberrant dermatoglyphics, it was hypothesized that individuals with "idiopathic" congenital heart disease without evidence of any extra-cardiovascular abnormalities might have abnormal dermatoglyphic patterns as well. The finding of an association between CHD and dermatoglyphics would aid in diagnosis, counseling, the study of familial CHD, and conceivably would help elucidate the role of various environmental and genetic influences in the etiology of CHD. The present study was designed to determine whether the dermatoglyphics of patients with CHD and of normal controls differ.

Subjects Studied

A total of 225 patients, 119 males and 106 females, with a diagnosis of congenital heart disease was studied. Patients were selected from the wards of the Variety Club Heart Hospital and the Pediatric Heart Clinic of the University of Minnesota Hospitals. These patients are categorized by type of CHD in table 1. Upon admission all patients received detailed clinical and roentgenographic evaluation by the pediatric cardiology section. The basis of diagnosis in the majority was by surgery or cardiac catheterization, or both. A control group of 200 males and 200 females was obtained from the University of Minnesota Cancer Detection Clinic, the hospital nursing and technical staffs, a student dormitory, and a National Guard facility. All subjects and controls were Caucasian. The dermatoglyphic values in the Minnesota normal series correspond closely to those from other dermatoglyphic research centers in Canada and the United States.

Table 1

<table>
<thead>
<tr>
<th>Type of defect</th>
<th>No.</th>
<th>Mean age</th>
<th>std angle*</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial septal defect</td>
<td>32</td>
<td>10.0</td>
<td>94.8 ± 3.7</td>
<td>&lt; 0.10</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>42</td>
<td>9.1</td>
<td>95.2 ± 3.0</td>
<td>&lt; 0.02†</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>16</td>
<td>7.6</td>
<td>101.1 ± 5.6</td>
<td>&lt; 0.05†</td>
</tr>
<tr>
<td>Coarctation of the aorta</td>
<td>16</td>
<td>10.4</td>
<td>91.7 ± 3.1</td>
<td>&lt; 0.20</td>
</tr>
<tr>
<td>Pulmonary stenosis</td>
<td>17</td>
<td>11.2</td>
<td>92.0 ± 3.4</td>
<td>&lt; 0.20</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>20</td>
<td>12.0</td>
<td>92.8 ± 3.4</td>
<td>&lt; 0.20</td>
</tr>
<tr>
<td>Atrioventricular canal defects</td>
<td>6</td>
<td>9.2</td>
<td>85.8 ± 3.3</td>
<td>&lt; 0.80</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>36</td>
<td>9.2</td>
<td>100.4 ± 3.9</td>
<td>&lt; 0.01‡</td>
</tr>
<tr>
<td>Transposition of great vessels</td>
<td>9</td>
<td>7.8</td>
<td>93.4 ± 3.7</td>
<td>&lt; 0.20</td>
</tr>
<tr>
<td>Endocardial fibroelastosis</td>
<td>2</td>
<td>11.0</td>
<td>77.5 ± 8.5</td>
<td>&lt; 0.20</td>
</tr>
<tr>
<td>Multiple defects</td>
<td>15</td>
<td>9.7</td>
<td>99.1 ± 4.5</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Tricuspid arteria</td>
<td>4</td>
<td>13.5</td>
<td>97.0 ± 13.8</td>
<td>&lt; 0.80</td>
</tr>
<tr>
<td>Other</td>
<td>10</td>
<td>13.0</td>
<td>93.4 ± 5.7</td>
<td>&lt; 0.50</td>
</tr>
<tr>
<td>Total</td>
<td>225</td>
<td>9.9</td>
<td>95.5 ± 1.3</td>
<td>&lt; 0.005§</td>
</tr>
<tr>
<td>Normal values</td>
<td>200</td>
<td>—</td>
<td>87.4 ± 1.8</td>
<td></td>
</tr>
</tbody>
</table>

*Values summed for both hands = SE.
†Significant.
‡Highly significant.
§Very highly significant.
Methods

Prints of the fingers, palms, great toe, and hallux were obtained by an inkless technic. A total of 10 dermatoglyphic features was analyzed and verified by two observers. The features included total finger ridge count; finger tip patterns; thenar-first interdigital pattern; second, third and fourth interdigital patterns; hypothenar pattern; transverse palmar flexion crease pattern; atd angle; a-b ridge count; hallucal pattern; and pattern on the great toe. The methods of classification outlined by Cummins and Midlo, the fingerprint manual of the Federal Bureau of Investigation, and Uchida and Soltan were used. All dermatoglyphic values and abstracts of clinical histories were transferred to data processing cards and analyzed by the Biomedical Computing Service of the University of Minnesota.

Each of the dermatoglyphic parameters was analyzed separately by sex and hand. Fingerprint patterns were classified as radial loops, ulnar loops, whorls, and arches. The subtypes of whorls and arches were not classified separately in this study. The mean value of pattern occurrence was computed by summing the types for each of the 10 fingers and dividing by the total number of individuals. Thus, each individual was counted once. The total finger ridge count for each subject was the sum of the ridge counts of the 10 fingers. With whorl patterns, only the highest of the two possible counts was used for computation of the total. Lines drawn from a to t to d outlined the angle atd. The most distal placement of t was used to record the angle atd. Values were summed for right and left hands to give one value per individual in calculating the mean atd angle for the group. In thenar-first interdigital and other interdigital areas, the presence or absence of pattern was indicated. Hypothenar patterns were classified as ulnar, radial, or carpal arches; ulnar, radial, or carpal loops; whorls; double, and other patterns. The ridges crossed by a line connecting the a and b triradii, which defined the a-b ridge count, were summed for the right and left hand so that one a-b ridge count was derived for each individual. Palmar flexion creases were classified as normal, transitional lines, or as a simian “four finger” line. The great toe patterns included arches, tubial or fibular loops, and whorls. The hallucal areas were classified as distal, tubial, or fibular loops; tubial, proximal, tubial, or tented arches; or whorls. The great toe and hallucal patterns on each foot were considered separately. A review published by Alter provides illustrations of these patterns.

Results

Although the congenital heart disease group tended to have a slight increase in the frequency of patterns in the fourth interdigital area, thenar-first interdigital areas of the palm, and a slightly higher frequency of double and other patterns in the hypothenar areas, these differences were not statistically significant. The total finger ridge count, a-b ridge count, finger pattern frequency, simian line frequency, and hallucal and great toe patterns were also similar for the two groups. Indeed the CHD group and the normal group were remarkably similar in dermatoglyphic configuration. However, the mean summed atd angle was greater in the CHD group than in the normal controls (table 1). This angle tends to decrease as the palm elongates with age and thus is wider in children than in adults. It is important, therefore, to note that the CHD group, although younger than the controls, was made up primarily of children of average age 9.9 years rather than infants and the atd angle of older children approximates that of adults. It is unlikely, therefore, that the large mean atd angle is attributable to the younger average age of the CHD group.

The atd angle in individual types of CHD was analyzed and results are shown in table 1. Patients with ventricular septal defect, patent ductus arteriosus, tetralogy of Fallot, and multiple defects had atd angles which were significantly wider than controls. With the exception of those found in atroventricular canal defects and endocardial fibroelastosis, the mean atd angle was wider in other types of CHD than in controls but statistical testing failed to show that the difference was significant.

Discussion

The present study is one of the largest in the literature that compares a normal control series with a group whose CHD was diagnosed not only by clinical criteria but, in many cases, by extensive roentgenographic studies and surgery. It also compared several features rather than a single dermatoglyphic feature. Of the dermatoglyphic features studied, the atd angle was found to be significantly wider in CHD than in normal controls.
Several previous studies of dermatoglyphics in CHD have been made. The earliest report by Hale and associates\textsuperscript{35} was published in 1961. They compared 157 patients who had different types of CHD with 143 patients who had acquired heart disease. A distally displaced axial triradius was twice as common in those with CHD. Distal axial triradii cause widening of the atd angle.

The same year, Rowe and Uchida\textsuperscript{36} reported that mongoloid children with CHD had a higher frequency of distally displaced axial triradii than did mongoloid children with normal hearts. However, distal axial triradii were found with higher frequency in both groups of mongoloids than in a normal population.

Fried and Neel,\textsuperscript{37} in a published abstract in 1962, commented on the higher frequency of wide atd angles and distal axial triradii in patients with CHD.

Of 15 patients with CHD studied by Christensen and Nelson,\textsuperscript{38} 11 (73\%) had distal or multiple axial triradii whereas only six of 25 (24\%) with acquired heart disease had this dermatoglyphic stigma.

Sanchez Cascos\textsuperscript{39-41} studied dermatoglyphics in 150 patients with CHD and in 50 controls. He observed a higher frequency of arches on finger tips in patients with pulmonary stenosis and an unusually high frequency of ulnar loops associated with ventricular septal defects. Radial loops were somewhat more common in patients with atrial septal defect, and whorls were more frequently associated with aortic stenosis, aortic coarctation, and tetralogy of Fallot. On the palms, wide atd angles occurred more often in patients with CHD, especially in the group with Fallot's tetralogy. Sanchez Cascos postulated that the patients with CHD who showed abnormal dermatoglyphics represented the fraction of CHD that was genetically determined.

Weninger and her associates\textsuperscript{42} reported a high frequency of whorls and a higher total ridge count in males with patent ductus arteriosus and in females with aortic stenosis. The A main line tended to follow a longitudinal course. In their series of CHD, the frequency of distal axial triradii was not significantly increased, but the frequency of hypothenar patterns was elevated.

Takashina and Yorifuji,\textsuperscript{43} studying Japanese and American subjects, observed a distal axial triradius in 64\% of 44 patients with CHD compared with 16\% of 362 patients with acquired heart disease. They had no normal control sample.

In a series by Emerit and co-workers\textsuperscript{44} consisting of 330 patients with CHD and 200 with acquired heart disease, distal axial triradii were present in about one third of the former and only one fifth of the latter. A single transverse palmar crease was significantly increased in those whose cardiac defect was associated with other congenital anomalies. Hypothenar patterns were increased in frequency. Arch patterns occurred less often in those whose cardiac defect was the only malformation detected. In 21 cases of familial cardiac defects, ulnar loops increased and whorl patterns decreased.

The most recently reported series published by Burguet and Collard\textsuperscript{45} consisted of 98 patients with CHD and 198 normal controls of similar age. Patients with ventricular septal defect and patent ductus arteriosus had distal axial triradii more often than did controls. Burguet and Collard pointed out that cardiac differentiation occurs embryologically between the third and the ninth week of gestation and dermatoglyphics differentiate between the seventh and twelfth week. Hence, anomalies which occur late in cardiac embryogenesis, such as ventricular septal defect, may logically be expected to be associated with dermatoglyphic abnormalities as was observed.

In the present study, a higher frequency of wide atd angles was observed in the patients than in the controls. This difference may be attributable to the fact that the CHD group consisted of children whereas the controls were adults. However, this variation in age is unlikely to be pertinent because the mean age of the CHD group was almost 10 years and the patients also had a higher frequency of
hypothenar patterns. Hypothenar patterns are associated with distal axial triradii and wider atd angles regardless of age. Therefore, the present study appeared to support the results of most previous studies that CHD may be associated with distal axial triradii. No statistically significant differences were observed in the other dermatoglyphic features analyzed. Analysis of dermatoglyphics in patients suspected of having specific types of CHD should be encouraged.

In the present study, analysis of dermatoglyphics in cases of specific cardiac defects revealed that the atd angle was significantly increased in ventricular septal defect, patent ductus arteriosus, tetralogy of Fallot, and in multiple defects but not in other types of CHD. However, in all but two of the other types, the mean value of the atd angle was higher than in the controls.

Dermatoglyphics develop during the end of the first trimester and the beginning of the second after much of the heart is already formed. However, the anlage of the ridges, the volar fat pads, are present earlier and it is conceivable that the factors present during a critical period of gestation may alter both the formation of the heart and the palmar ridges. Alternatively, a genetic factor may determine both the occurrence of certain types of heart disease like tetralogy of Fallot and ventricular septal defect and the position of the axial triradius. Evidence to support either of these conjectures is lacking at present.

Of those investigators who have studied dermatoglyphics in specific types of CHD, Burguet and Collard\(^45\) observed an increased atd angle or distal axial \(t\) in ventricular septal defect and patent ductus arteriosus. Sanchez Cascos\(^46\) reported it in Fallot's tetralogy, and Emerit's group,\(^44\) in a variety of specific defects. In many of these series, the number of cases of each type of defect was small. Even in the present study, which included a rather large sample, sufficient cases of only a few of the cardiac defects were available to make a detailed statistical analysis worthwhile.

Although not all studies agree as to which specific type of CHD is associated with widened atd angle, almost all investigators concur that this dermatoglyphic parameter is abnormal in CHD. The approximate juxtaposition in time of cardiac and dermatoglyphic differentiation makes it entirely plausible that defects in one may be associated with defects in the other more often than by chance. Abnormal dermatoglyphics, especially the atd angles, may yet provide a clue to the identification of that subgroup of CHD due to a genetic cause or to a teratogen operating during early gestation when both the heart and the skin ridges are forming.

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