Diagnostic Import of QRS Notching in High-Frequency Electrocardiograms of Living Subjects with Heart Disease

By Nancy C. Flowers, M.D., and Leo G. Horan, M.D.

SUMMARY
In a 10-month period 92 patients have been studied for the occurrence of high-frequency notching in orthogonal electrocardiographic leads X, Y, and Z obtained by high-frequency, high-speed techniques. The same patients were studied radiographically with barium, with routine electrocardiograms, hemodynamically at cardiac catheterization and, in many instances, with left ventricular angiograms. Sixty-nine patients had not had cardiac surgery prior to recording and had normal duration of ventricular activation. These patients were placed into groups which included those with no ventricular enlargement, isolated right ventricular enlargement, isolated left ventricular enlargement, and biventricular enlargement.

The patients with no ventricular enlargement had a mean of 2.9 notches and never exceeded a total notch count of 6. Those with single ventricular enlargement had a mean of between 5 and 6, while those with biventricular enlargement frequently exceeded 6 notches and had a mean of 8.6. The differences were statistically significant.

We concluded, then, that notch count correlates well with the dynamic evidence of ventricular enlargement in a living population. Since the effect is additive, biventricular enlargement elevates the counts sufficiently to remove the overlap with normal seen in groups with univentricular enlargement.

Additional Indexing Words: High-frequency components Ventricular hypertrophy

Since the early 1950's efforts have been made intermittently to correlate the occurrence of high-frequency notching in the electrocardiogram (ECG) with clinical disease states. The association with atherosclerotic heart disease and myocardial scarring, primary myocardial disease, and ventricular enlargement (VE) has been clearly established.1-16 Some increased frequency of loop distortion in a group of nonautopsied diabetic subjects has also been reported.17

Because most of the early studies by necessity were without anatomic findings, our original studies were undertaken to supply this correlation.13, 14 In these the investigators personally performed each dissection and separately tabulated each high-frequency examination. Several interesting conclusions resulted: It was clearly established that VE had as high a notch count associated with it as did myocardial scarring. Both groups were clearly separable from normal by notch count alone without any other consideration in the QRS complex or loop. The patients with isolated left or isolated right ventricular enlargement (LVE and RVE) had elevated counts but did not seem to have counts as high as those with

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Supported by an award from the Veterans Administration, U.S. Public Health Service Grants HE-11667 and HE-09495, and Research Grant 69-783 from the American Heart Association.
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Received December 14, 1970; revision accepted for publication June 7, 1971.
biventricular enlargement (BVE). The number of such subjects with enlargement of a single ventricle was relatively few, however, and the average age of all subjects with enlargement was relatively high (59 years). Therefore, we were prompted to study the present group of patients referred to the Medical College of Georgia for cardiologic evaluation. The primary etiologies in the group previously studied had been systemic hypertension and primary or secondary myocardial disease. Because the current group under study was heavily weighted with patients with congenital and acquired valvular lesions, we expected to see a younger mean age than before and many more instances of single-chamber ventricular enlargement. We felt that this would permit us to determine whether the clearly elevated notch count in BVE, the intermediately high notch count in RVE or LVE, and the low notch count in normal-sized hearts were associations which hold for a carefully studied living population as well as for a population selected by autopsy.

Methods

From May 16, 1969 to March 12, 1970, 92 patients were studied in the vectorcardiographic laboratory of the Eugene Talmadge Memorial Hospital. Vectorcardiograms and orthogonal leads X, Y, and Z of the electrocardiogram were recorded by the Helm system18 on an Electronics for Medicine photographic recorder at 200 mm/sec at a frequency response of 0.1 to 2,000 Hz. After elimination of subjects with QRS complexes of 0.12 second duration or longer or cardiotomy prior to recording X, Y, and Z leads, 69 remained for inclusion in the correlative studies.

Notches and slurs in the QRS complex were counted by techniques previously described.6,13,14 Because one did not occur without the other, notches and slurs were considered together in a report of notch count. To be included in the count, each departure from the smooth slope of the QRS complex was required to appear in three consecutive beats at the same instant during the
QRS NOTCHING

Table 1

Etiologies of Heart Disease in Ninety-Two Patients

<table>
<thead>
<tr>
<th>Etiology</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatic</td>
<td>36 (11)*</td>
</tr>
<tr>
<td>Congenital</td>
<td>21 (4)</td>
</tr>
<tr>
<td>Atherosclerotic heart disease</td>
<td>9 (1)</td>
</tr>
<tr>
<td>Systemic hypertension</td>
<td>2</td>
</tr>
<tr>
<td>Traumatic</td>
<td>3 (1)</td>
</tr>
<tr>
<td>Primary pulmonary hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Luetic</td>
<td>1</td>
</tr>
<tr>
<td>Pericardial cyst</td>
<td>1</td>
</tr>
<tr>
<td>Uncertain Etiology</td>
<td></td>
</tr>
<tr>
<td>Calcific aortic stenosis</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Aortic insufficiency with root disease</td>
<td>5 (2)</td>
</tr>
<tr>
<td>Idiopathic cardiomyopathy</td>
<td>5 (1)</td>
</tr>
<tr>
<td>Idiopathic hypertrophic subaortic stenosis</td>
<td>2</td>
</tr>
<tr>
<td>Hyperkinetic heart syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Undiagnosed</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>92 (23)</td>
</tr>
</tbody>
</table>

*The numbers in parentheses indicate subjects from each etiology eliminated from correlative study because of prolongation of the QRS to 0.12 sec or more, the absence of normal sinus rhythm, or cardiomyopathy prior to recording.

Results

In figure 1 can be seen an example of the raw data from which notch counts were obtained. The orthogonal leads X, Y, and Z are shown from a subject with no VE (fig. 1a), single VE (fig. 1b), and BVE (fig. 1c). Notching is indicated by arrows. (Note that the polarity of the Z lead is the reverse of that usually reported; upright deflections indicate activation directed anteriorly and downward deflections indicate activation directed posteriorly.)

Table 1 shows the etiologies of heart disease in the original 92 patients from whom data were obtained. The 23 patients indicated in parentheses are not included in the correlative studies because of conduction defects or cardiomyopathy.

Table 2 illustrates the low mean notch count in the 13 patients without VE, the somewhat higher mean notch count in the 39 patients with single VE, and the clearly higher notch count in the 17 patients with BVE. Mean ages are also shown. There is no significant statistical difference in ages.

Figure 2 shows the distribution of the data for each group and indicates that in no instance did any patient in the group without VE demonstrate a notch count higher than a total of 6 for X, Y, and Z combined. Skewing is apparent. In the case where no Gaussian or normal distribution is assumed, one can at least examine whether the number of notches differs significantly for the different categories by the extension of the median test.28 The chi-square calculation based on this approach led to the conclusion that the number of notches does differ significantly for the different groups ($X^2 = 18.60$ with 3 degrees of freedom: $P < 0.001$).

The effect of the distribution of these samples on such classic parametric approaches as analysis of variance is difficult to estimate—if not impossible—because the normal distribution is assumed by the method of data analysis. However, it is worthwhile to examine an analysis of variance as applied to these data28 (table 3). After first determining that variance was homogeneous and that significant differences existed between the means.
Table 2

<table>
<thead>
<tr>
<th>Notch Count</th>
<th>No. of subjects</th>
<th>Mean age ± sd</th>
<th>Mean notch count ± sd</th>
<th>Notch count, median</th>
</tr>
</thead>
<tbody>
<tr>
<td>No VE</td>
<td>13</td>
<td>33.5 ± 11.7</td>
<td>2.9 ± 1.9</td>
<td>2.3</td>
</tr>
<tr>
<td>RVE</td>
<td>13</td>
<td>32.2 ± 14.5</td>
<td>5.0 ± 1.9</td>
<td>4.7</td>
</tr>
<tr>
<td>LVE</td>
<td>26</td>
<td>40.7 ± 14.2</td>
<td>5.2 ± 1.8</td>
<td>5.8</td>
</tr>
<tr>
<td>BVE</td>
<td>17</td>
<td>36.5 ± 14.3</td>
<td>8.6 ± 2.9</td>
<td>8.2</td>
</tr>
<tr>
<td>Total</td>
<td>69</td>
<td></td>
<td>5.6 ± 2.9</td>
<td>5.6</td>
</tr>
</tbody>
</table>

Abbreviations: VE = ventricular enlargement; RVE = right ventricular enlargement; LVE = left ventricular enlargement; BVE = biventricular enlargement.

(P < 0.001) as with the medians, we set up the 2 × 2 table to assay the effect of each ventricular enlargement upon mean notch count. As shown in table 3, interaction (antagonism or cancellation of effect) between the right and left ventricular enlargement could not be demonstrated. The unbiased estimate of the mean effect of right ventricular enlargement was that it added 2.9 notches; similarly, the mean effect of left ventricular enlargement was an increase of 3.0 notches. Both estimates were highly significant.

Discussion

We have become increasingly convinced that the counting of high-frequency notches may be a precise means of separating normal from abnormal subjects. When a total of 6 notches in X + Y + Z combined is exceeded, a careful search should be made for cardiac disease. We previously noted that the scalar orthogonal leads of an occasional subject without enlargement or detectable scarring contained 7 notches. This occurrence was rare in our previous study and did not occur in the present one. In our experience 8 notches and above have uniformly related to either the presence of VE or myocardial scarring—and the larger the two chambers of the heart, the higher the notch count becomes.

There is some overlap between the total notch counts of the subjects with single VE and the normal subjects (fig. 2). The counts of individuals with single ventricular enlargement tend to cluster in the range of 5 or 6 notches, while the counts from those with no VE tend to peak in the region of 1 or 2 notches. Likewise, in this particular study, no patient with BVE had less than 5 notches, while many manifested 7 and above. These findings present a practical problem in using notch count as a screening criterion. Defining diagnostic accuracy as the percentage of true negatives plus true positives in the total population, we may examine the relative value.
Table 3*

2 × 2 Table for Ventricular Enlargement

<table>
<thead>
<tr>
<th></th>
<th>No VE</th>
<th>RVE</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$n_1$</td>
<td>$\bar{x}_1$</td>
<td>$n_2$</td>
<td>$\bar{x}_2$</td>
<td>$W = \frac{n_1 n_2}{n_1 + n_2}$</td>
</tr>
<tr>
<td>No VE</td>
<td>13</td>
<td>2.85</td>
<td>13</td>
<td>5.00</td>
<td>6.5</td>
</tr>
<tr>
<td>LVE</td>
<td>26</td>
<td>5.23</td>
<td>17</td>
<td>8.65</td>
<td>10.28</td>
</tr>
</tbody>
</table>

Sum of squares for interaction = $\Sigma WD^2 - \frac{(\Sigma WD)^2}{\Sigma W} = 150.29 - \frac{(49.13)^2}{16.78} = 6.44$

$F = \frac{6.44}{4.50} = 1.43$ (not significant)

Correction for disproportion = $(\text{Sum of squares for RVE}) - \frac{(\Sigma WD)^2}{\Sigma W}$

For LVE:

$76.61 - (-101.85) = 178.46$

Analysis of Variance

<table>
<thead>
<tr>
<th>Source</th>
<th>Degree freedom</th>
<th>Preliminary sum of squares</th>
<th>Corrected sum of squares</th>
<th>Mean square</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVE</td>
<td>1</td>
<td>42.00</td>
<td>143.85</td>
<td>143.85</td>
</tr>
<tr>
<td>LVE</td>
<td>1</td>
<td>76.61</td>
<td>178.46</td>
<td>178.46</td>
</tr>
<tr>
<td>Interaction</td>
<td>1</td>
<td>133.88</td>
<td>6.44</td>
<td>6.44</td>
</tr>
<tr>
<td>Individuals</td>
<td>65</td>
<td>292.19</td>
<td></td>
<td>4.50</td>
</tr>
</tbody>
</table>

For RVE, $F = 143.85/4.50 = 31.96$ (significant: $P < 0.001$)

Unbiased estimate of mean effect on notch count = $\frac{\Sigma WD}{\Sigma W} = \frac{49.13}{16.78} = 2.92$

For LVE, $F = 178.46/4.50 = 39.66$ (significant: $P < 0.001$)

Unbiased estimate of mean effect on notch count = $\frac{\Sigma WD}{\Sigma W} = \frac{47.53}{16.04} = 2.96$

*This table shows the result of analysis of variance when (1) the possibility of separate effects on the notch count from right and left ventricular enlargement (RVE and LVE) was entertained; and (2) allowance was made for the disproportionate numbers in the subclasses with no, right, left, and combined ventricular enlargement (VE). The treatment follows that of Snedecor, pages 379-382.

$F$ is the ratio of variances, in this instance the ratio of the "mean" square of deviations from the mean value in a specific subgroup to the mean square of deviations from the mean value for individuals in the whole population. In each case the mean squares are determined by dividing the sum of the squares of the deviations by the appropriate number of degrees of freedom; a subgroup consequently has only one degree of freedom and the "mean square" equals the square of deviations. The correction term is an unbiased estimate of the mean square between column means (RVE) and thus leads to the correction for disproportion when subtracted from the sum of squares for RVE. Reference to a table of distribution of F values permits estimate of the significance of the weighted mean difference in notch count by a specific ventricular enlargement. The estimate of the mean effect of LVE (last line in the table) was permitted by interchanging rows and columns to recalculate WD and W appropriately.

Abbreviations: $n_1$ and $n_2$ = the number of subjects; $\bar{x}_1$ and $\bar{x}_2$ = the mean notch count in the respective groups.

of cutoff points in the notch count. If we are trying to separate normal from abnormal and include in the latter both single and combined ventricular enlargement, diagnostic accuracy falls from 65% (with 5 notches or less as the normal cutoff) to 51% (with 6 or less) to 35% (with 7 or less). On the other hand, if we are merely interested in detecting biventricular enlargement the diagnostic accuracy rises in the same range from 67% to 78% to 88%.

Circulation, Volume XLIV, October 1971
Regardless of the statistical assumptions about distribution in the samples, the differences between the groups were significant, whether they were tested parametrically or nonparametrically. Unfortunately, a ready, applicable, and agreed-upon assay for interaction or additive effect is not at hand if we are unable to assume an underlying normal or Gaussian distribution. However, we examined the data by analysis of variance and the results were reasonable and interesting. It seems likely to us that they are probably also appropriate to the situation at hand if one is willing to relax the rigid demand for Gaussian distribution.

With such proviso, the analysis of variance indicated that the mean effect of enlargement of either ventricle would be to increase the number of notches by 3—not producing a clear separation from patients without ventricular hypertrophy. However, since the effect was additive, the group with biventricular hypertrophy emerged as distinct from the relatively normal group. Previous study of older subjects coming to autopsy suggested the intermediate state of univentricular enlargement between the group with biventricular enlargement and the group with none. There were insufficient numbers in the isolated ventricular enlargement category, however, to indicate the independent and additive effect of right and left enlargement as suggested here.

It is gratifying that in this study of much younger subjects with different etiologies of heart disease, the conclusions appear to be otherwise essentially the same as in the group of older subjects examined at autopsy. It is likely that as larger numbers of patients are studied isolated exceptions will be found; that is, patients with BVE with few notches and patients with no VE or scarring with many notches. We believe, however, that exceptions with deep overlap into inappropriate territories will be few and that the general discriminatory power between no VE and BVE or scar on the basis of high-frequency notch count alone will remain valid. When automated and combined with other indices, as perhaps those from a screening phonocardiogram, the criterion of high-frequency notch count may offer the additional jump in diagnostic effectiveness necessary for a high degree of screening accuracy in surveying large populations for heart disease.

Acknowledgment

We appreciate the contributions made by Mrs. Pat Orander, Mrs. Mary Walden, Mr. Carey Miller, Mrs. Hazel Wall, and Mrs. Beryl Wilson in the preparation of this manuscript, and the assistance in data collection provided by Dr. John Edmonds and Dr. A. Calhoun Witham.

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Circulation. 1971;44:605-611
doi: 10.1161/01.CIR.44.4.605

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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