Study of Ventricular Response in Atrial Fibrillation

By Leo G. Horan, M.D., and Jack C. Kistler, M.D.

Physicians have long reflected upon the irregularity of pulse in patients with atrial fibrillation. The peculiar ventricular response found in atrial fibrillation provokes such questions about the nature of conduction from atrium to ventricle as, for example: Is the ventricular rhythm absolutely irregular? If there is not a random distribution of the varying time interval between beats, does a repetitive pattern emerge—or, at least, is there more than one favored ventricular interval recurring with disproportionate frequency? Why is there frequently such a wide range in the ventricular interval? Sometimes the variation in time between ventricular beats is from 0.4 to 1.5 seconds—a far greater variation than would be expected from a simple recovery period for the atioventricular node and ventricles (0.2 to 0.4 second) with a varying addition from an atrial interval of about 0.15 second.

The question of a hidden pattern in the ventricular irregularity accompanying atrial fibrillation has been raised previously.1-5 If no such pattern is present, then a plot of the frequency distribution of R-R intervals should result in a more-or-less normal single-peaked curve as found by Jordan5 but not by Arnoldi1 or Söderström.2 Because the previous studies were conflicting or inconclusive, the present work was undertaken to re-examine this possibility in greater detail by measuring the frequency distribution of the R-R interval in atrial fibrillation. In many instances, more than one clearly defined peak or mode was found, suggesting that ventricular activation was initiated in a non-random manner.

Methods

The lead showing the most clearly defined QRS complex (usually lead II) was recorded for relatively long durations varying from 442 to 1,412 beats in 17 patients with atrial fibrillation. In some patients several recordings were obtained so that a total of 47 records were analyzed. The R-R intervals were measured to the nearest 0.01 second for each beat with care that, in instances of change of form of the QRS complex, the intervals measured were exactly from onset-of-QRS to onset-of-QRS. To minimize measuring error, the data were grouped into 0.02-second intervals for analysis.

For each period of observation, distribution curves were plotted showing the percentage of the total number of beats for each group of R-R interval lengths. Consecutive observations on the same patient were compared with regard to the configuration of the distribution curves, and the configurations of all curves were examined with attention to the mean ventricular rate of each.

Results

Several distinctive patterns of frequency distribution curves of the R-R interval in atrial fibrillation were observed. There were 28 curves with a single peak varying from the tall and narrow, as seen in the top graph of figure 1, to the short and broad, as seen in the fourth graph of figure 1 or the third graph in figure 2. All but three unimodal curves were skewed with tailing to the right. Among the 11 bimodal curves, there was great variation in the relative size of the two peaks, as noted in the second and third graphs of figure 1. Finally, there were two less common configurations: a high plateau-like curve in five instances and three long, low, flattened curves (bottom graph of fig. 2).

Serial observations were obtained in 10 patients with pronounced changes of configuration in the distribution curves in the same individual under different clinical circumstances. In figure 1 are five graphs de-
Serial graphs of the distribution of R-R intervals in a 71-year-old woman with arteriosclerotic heart disease and atrial fibrillation who was undergoing digitalization. Note the initial peak near 0.40 second, then the appearance of a second peak between 0.60 and 0.70 second, and finally the presence of the second peak alone until the rate was increased with atropine.

The series of graphs in figure 2 differs in several respects. The first two graphs were taken five and nine days respectively after removal of digitalis from the patient's therapy; both curves are bimodal with the short-interval peak dominant at the faster rate. However, upon administration of quinidine (third graph), a rate intermediate between the two previously observed was accompanied by a single-peaked curve. (Similar "normalization" of the distribution with quinidine was also noted in the one other patient receiving the drug.) Upon subsequent digitalization to toxicity, a long flattened curve was obtained, but after a few days a late unimodal curve was found. The two graphs of 9/30/58 show a marked change in configuration following the administration of atropine (0.001 Gm.)—from unimodal to bimodal curve; the two peaks were very close in location to the intervals at which the two previous modes were found (near 0.40 and 0.60 second) on 9/16 and 9/20/58.

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 Relation Between the Distribution of Ventricular Intervals and Rate

Further study of the distribution curves revealed a common characteristic of the double-peaked curves: they nearly all fell within a middle range of mean ventricular rates. As seen in figures 3 and 4, when peaks of the curves were plotted against the average ventricular rate, double-peaked curves were seen between 120 and 90, with three exceptions. Several plateau-like configurations were noted at rates of about 100 beats per minute.

Such an ordering by rate was more apparent in given individuals in the progression from unimodal through bimodal to flattened curves upon the administration of digitalis (or in the retrogression with atropine). The possibility that the bimodal record might be an artifact from the overlapping of a period of fast rate with one of slow rate was checked by noting the distribution curve formed by each consecutive 100 beats. No great departure from the basic curve was found in any instance.

QRS Complexes of Altered Form

In 22 of the 49 records, there were no gross alterations of configuration in the QRS complex other than the small changes in amplitude frequently seen with atrial fibrillation (table 1). There were 13 records with fewer than 1 per cent of the QRS complexes altered or aberrant in form; 11 records with fewer than 5 per cent but more than 1 per cent; and only one record with more than 5 per cent. The number of different kinds of variant QRS configurations appearing on any one record varied between one and five. The frequency of premature beats did not appear in general related to the mean ventricular rate or configuration of the distribution curve (table 1).

Relation Between Successive R-R Intervals

The question arose of whether certain repeated associations of cycle length occurred more frequently than might be expected by chance. For example, was there an inordinately large number of intervals of 0.70 second immediately following those of 0.42 second? To examine this possibility, distribution curves of the R-R intervals were plotted for each given preceding R-R interval in five bimodal recordings. The resulting secondary, or daughter, distribution curves
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Heart size</th>
<th>Total mean ventricular heart rate</th>
<th>Peak ventricular heart rate</th>
<th>Interval</th>
<th>Altered heart sounds</th>
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<tbody>
<tr>
<td>LJ</td>
<td>62F</td>
<td>HCVD, DM</td>
<td>654</td>
<td>60</td>
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<td>None</td>
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<tr>
<td>JAL</td>
<td>72M</td>
<td>ASHD</td>
<td>1100</td>
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<td>WWH</td>
<td>44M</td>
<td>RHD, MS</td>
<td>504</td>
<td>57</td>
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<td>None</td>
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<tr>
<td>PS</td>
<td>38M</td>
<td>ASHD</td>
<td>1000</td>
<td>86</td>
<td>86-60</td>
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<tr>
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<td>728</td>
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<tr>
<td>WKL</td>
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<td>ASHD</td>
<td>725</td>
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<tr>
<td>WEL</td>
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<tr>
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<td>755</td>
<td>100</td>
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<tr>
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<td>67M</td>
<td>ASHD</td>
<td>725</td>
<td>86</td>
<td>None</td>
<td>None</td>
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</tbody>
</table>

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were compared as to configuration with the
mother curve of distribution and were rough-
ly the same in records with few or no aber-
rant QRS complexes. Such similarity suggests
that recurrent associations were merely the
results of random selection from the avail-
able population.

An exception to the apparent random
association of adjacent intervals was noted
in the one record in which a significantly
large proportion (20 per cent) of variant
QRS complexes occurred (patient L. B. in

Historical Considerations

Arnoldi 1 made serial comparisons at vary-
ing average heart rates in patients with atrial
fibrillation who were undergoing digitaliza-
tion, and reported two peaks in the distribu-
tion of R-R intervals, with a tendency for
10 patients with atrial fibrillation. A similar
grouping about the short, "dominant" inter-
vals at fast rates and about the long, "domi-
nant" intervals at slower rates. Jordan 5 failed
to get multiple peaks in longer records from
10 patients with atrial fibrillation, with a tendency
for grouping about the short, "dominant" inter-
vals at slow rates and about the long, "domi-
nant" intervals at fast rates. Soderstrom 2 plotted
R-R intervals against consecutive beat number in 100-beat
electrocardiographic traces of patients with
atrial fibrillation or atrial flutter, he noted
"levels" about which the intervals seemed
to group with change in the proportion of
the intervals found at the different levels
upon exercise. Because atrial fibrillation
was different from atrial flutter in that the domi-
nant R-R intervals did not appear to be
multiples of the atrial period (P-P or P-F
interval), he postulated that the levels in
atrial fibrillation were multiples of the refrac-
tory periods. However, the intervals found at the diff-
erent "levels" were not multiples of the refrac-
tory period. Therefore, the "levels" observed by
Soderstrom 2 were not the same as those
observed by Arnoldi 1.

Discussion

An exception to the apparent random
association of adjacent intervals was noted
in the one record in which a significantly
large proportion (20 per cent) of variant
QRS complexes occurred (patient L. B. in

<table>
<thead>
<tr>
<th>MP</th>
<th>62M</th>
<th>ASHD</th>
<th>9/15/58</th>
<th>None</th>
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<th>97</th>
<th>0.56</th>
<th>0.36-0.96</th>
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<tr>
<td>LR</td>
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<td>RHD / e AS &amp; AI</td>
<td>10/11/58</td>
<td>Digitalis</td>
<td>1018</td>
<td>80</td>
<td>0.74</td>
<td>0.46-1.14</td>
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<tr>
<td>RWE</td>
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<td>ASHD, CP</td>
<td>10/21/58</td>
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<td>979</td>
<td>75</td>
<td>0.78</td>
<td>0.46-1.44</td>
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<tr>
<td>MY</td>
<td>60M</td>
<td>ASHD</td>
<td>1/15/59</td>
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<td>0.36-1.00</td>
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<tr>
<td>WCV</td>
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<td>RHD / e MI (ASHD)</td>
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<td>Frequency</td>
</tr>
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<td>HCVD, ASHD</td>
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<td>500</td>
<td>165</td>
<td>0.28</td>
<td>0.26-0.62</td>
<td>Rare</td>
</tr>
<tr>
<td>LR</td>
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<td>RHD / e MS</td>
<td>7/28/58</td>
<td>Digitalis</td>
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<td>100</td>
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<td>0.32-1.18</td>
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<tr>
<td>TV</td>
<td>50M</td>
<td>RHD / e MS</td>
<td>1/16/59</td>
<td>Digitalis</td>
<td>753</td>
<td>83</td>
<td>0.50-0.76</td>
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</tr>
</tbody>
</table>

*HCVD = hypertensive cardiovascular disease; ASHD = arteriosclerotic heart disease; RHD = rheumatic heart disease; MS = mitral stenosis; MI = mitral insufficiency; AS = aortic stenosis; AI = aortic insufficiency; CP = cor pulmonale; DM = diabetes mellitus.
†Four days after stopping digoxin.
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Figure 5

Graphs of the distribution of R-R intervals from two subjects with atrial fibrillation. The graphs show the distribution of QRS complexes of altered form. Two variant forms appeared after relatively short ventricular intervals in each, but only in the second were the altered complexes so numerous as actually to constitute a distinct peak. At about 0.40 second, the first peak for (L.B.) was composed principally of intervals terminated by a 0.13-second, LBBB-like QRS complex (a) and followed by relatively long intervals (mostly over 0.56 second). By contrast, the interval preceding the interval terminated by the later 0.11-second, RBBB-like variant (b) was consistently long (over 0.54 second), but no pattern was detected for the succeeding interval.

The more fundamental question not answered here is whether there is a more complex interrelationship between several various-sized intervals or intervals more remote from one another in time than those of adjacent beats. A search for such autocorrelation is certainly needed for the further study of possible hidden patterns in the ventricular response to atrial fibrillation, but is beyond the scope of the present analysis.

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Relation to Ventricular Rate

When the ventricular rate at which each frequency distribution curve of ventricular intervals was considered, a general pattern emerged (fig. 4). Omitting instances in which quinidine had been administered, the ventricular intervals in atrial fibrillation appeared (a) to cluster about a single narrow peak at rates above 140, (b) to group about two peaks at intermediate rates, and (c) to fall again within a second peak or within a long, low curve at rates lower than 90. The relationship of configuration to ventricular rate was certainly more convincing as an ordered progression in the individual patient (figs. 1 and 2) than in the whole group (fig. 4).

Regardless of the mechanism—whether by partial nodal penetration3 or dual nodal pathway4—some form of concealment of impulses in the A-V nodal system is suggested by the data as presented in figure 4. At fast ventricular rates, the R-R interval appears largely a function of the effective refractory period of the ventricles. With increasing vagal stimulation or administration of digita
dalis, the opportunity for concealment of an impulse may be progressively increased until finally every conducted impulse follows an interval that contains one or more concealed impulses. The manner of ventricular slowing demonstrated in this study is thus progressive shifting from ventricular intervals containing one major refractory period to those containing two or more such refractory periods.

The exact mechanisms of A-V nodal conduction in atrial fibrillation are as yet poorly defined, but tentative answers to the questions raised at the onset may be offered: The irregularity in atrial fibrillation is not absolute or random; instead, the ventricular intervals usually cluster about modes (probably determined by the A-V nodal refractory period). Changes in mean ventricular rate frequently occur with a relative increase or decrease in the number of short or long ventricular intervals rather than by the diffuse lengthening or shortening of all the intervals. The fact that such a mixture of distinct families of intervals frequently occurs may also help, in part, to explain the wide variation in length of the ventricular interval noted at any given time of observation.

Summary

A study was made of the variation in R-R interval in 47 long electrocardiographic recordings from 17 patients with atrial fibrillation. The distribution curve of ventricular intervals was found to vary in configuration according to the mean ventricular rate. A single high peak was seen at fast rates, two peaks at intermediate rates, and a single low peak flattening to a long low curve at slow rates.

Acknowledgment

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