distribution. More important, however, the possible existence of correlation among data was not addressed. It is generally known that correlation among data would seriously affect the results of analysis of variance. Therefore, it may be more appropriate to use a time series of analysis technique rather than the analysis of variance method.

From the computational formula of the 95% confidence limit for the difference between the control and test periods (which appears to have a typographical error), it is apparent that the authors assumed that variances during control and test periods are the same. If the therapeutic intervention, however, reduces VPD frequency during the test period, the variability of these readings also may be reduced dramatically. Therefore, the logarithmic or square root transformation would not be sufficient to create variance homogeneity in comparing the two groups of data. The well-known Behrens-Fisher problem would invalidate this computational formula.

The authors unfortunately did not address the question of variability of complex ventricular arrhythmias (multifocal VPDs, couplets or ventricular tachycardia) since the control of these arrhythmias may be more significant in the assessment of the efficacy of antiarrhythmic therapy than VPD count alone.

It would perhaps be most helpful if the authors would provide the original data for statistical reanalysis.

The authors reply:
To the Editor:

We were pleased to see the interest that Drs. Stein and Lee showed in our manuscript. Statistical analysis of our data required careful consideration because of its complexity, and we are happy to provide additional methodological data as requested by Stein and Lee.

The range of variability in our Holter data analysis system was 0.5–18% (average 7.2%). More important, the results of our analysis of variance technique did include the system variability which could not be fully discussed in our lengthy Methods and Results sections. Table 2 listed the sources of variation in ventricular ectopic frequency, and the “between hours” source of variation of 16% included the system variability. The data loss from Holter monitoring over 72 continuous hours in 15 patients was, surprisingly, not high. Only one patient (no. 15) had a total loss of data during 1 day, as noted in table 1. Two of the additional 14 patients had a loss of 10 and 6 hours during one of the 3 days of monitoring, while all other patients had only an occasional hour of lost data during the 72 hours of monitoring.

In our initial statistical analysis, we used both the square root and logarithmic transformation. From this comparative analysis, it was clear that the logarithmic transformation produced a better scale of measurement in which the “normality assumption” was more closely satisfied. However, in other sets of data, one should use both the square root and logarithmic transformations to determine which method produces the best analysis. We do not believe that time series analysis technique is best suited for analysis of our data due to the unavoidable presence of missing data inherent in any 24-hour Holter monitoring system. The statistical technique of evaluating data which is not complete by time series analysis has not been fully developed. We were gratified that, using either statistical approach, the basic fact of a high degree of spontaneous variability of ventricular ectopy was confirmed. In addition, the output of time series analysis would not have been as clinically relevant to physicians as the data derived from the analysis of variance that we employed.

The computational formula for the 95% confidence limit is correct as stated. However, the word “control” was omitted from the sentence: “Therefore, eD = test” which should have read: “Therefore, eD = test – control.” We agree that our assumption that the variability of ventricular arrhythmias during the test and control periods was uniform may not always hold. However, we chose to be conservative so as not to overstate our results since, if the variability decreases during intervention, we might have been able to detect even smaller differences than we reported. In addition, our variance components were obtained from individuals who met the entrance criteria of having a minimum of 30 ventricular premature depolarizations per hour during the 72 hours of monitoring. In a separate study which we did not detail, we found that the variance components were not altered by accepting individuals with entrance criteria of less than 30 ventricular premature depolarizations per hour. Obviously, further studies are needed to quantify the level of variability during the control vs test periods before this point can be resolved.

We agree that the variability of complex ventricular arrhythmias is an important consideration, and we have recently concluded our analysis of data to answer this question. In essence, we will soon be reporting a similar degree of spontaneous variability in complex arrhythmias which will require similar degrees of reduction for the achievement of a statistically significant change.

As always, our original data will be available to any interested individual on request.

Reference


The authors reply:

To the Editor:

The case report of Jeleeh et al. (Circulation 58: 747, 1978) suggests that the diastolic murmur noted in their patient with complete atrioventricular block originated from antegrade flow across a closing intrinsically normal mitral valve. As noted by the authors, a diastolic murmur is not present in the majority of patients with complete atrioventricular block. They advance the thesis that in a non-compliant left ventricle in their patient resulted in more rapid closure of the mitral valve leaflets while antegrade flow across the valve was still in progress, producing a diastolic murmur. The echocardiograms of their patient deserve further comment. The anterior mitral valve leaflet displays a markedly diminished E-F slope. This finding has been noted commonly in association with hypertrophic ventricles with diminished compliance. In addition, however, the anterior mitral valve leaflet in this case appears thickened, and the posterior leaflet appears to have restricted diastolic motion, both consistent with the presence of organic mitral stenosis. One wonders whether this patient, rather than having senile calcific aortic stenosis, in fact had rheumatic bivalvular disease. The onset of complete heart block, resulting in randomly timed atrial systole with intermittent obiligate blood flow across a partially closed, stenotic atrioventricular valve might lead to the exposure of previously “silent mitral stenosis.”

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Diastolic murmur of complete heart block.
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