LETTERS TO THE EDITOR

- *The British Heart Journal welcomes letters commenting on papers that it has published within the past six months.*
- *All letters must be typed with double spacing and signed by all authors.*
- *No letter should be more than 600 words.*
- *In general, no letter should contain more than six references (also typed with double spacing).*

Decreased heart rate variability in survivors of sudden cardiac death not associated with coronary artery disease

SIR,—Lü Fei *et al* showed decreased heart rate variability in survivors of sudden cardiac death not associated with coronary artery disease.[1] We, however, find it difficult to accept these conclusions in view of the slightly inappropriate statistical test that they used.

Lü Fei *et al* did not find statistically significant differences when they used the *t* test on 24 hour averaged heart rate variability values in the two groups. So they studied the hourly variability by pooling the hourly data of the patients and of the controls and using the *t* test again. We believe that pooling the hourly data for a group is incorrect because each patient has his/her own specific range of variability, where each value correlates with the following data points to some degree. A time series analysis based on the auto-regressive integrated moving averages technique would be more appropriate for data from repeated measurements on the same individual.[2]

Secondly, it is important that the two groups should not differ other than in the independent variable. As both groups had been exposed to routine activity, we assume that there may have been a difference in the level of activity in the group that had sudden cardiac death and the control group. It is essential that both the groups had the same level of activity, otherwise differing external stimuli would result in different degrees of sympathetic activation. This becomes especially important for comparisons of smaller subdivisions such as hourly intervals. Moreover there is variation in hourly heart rate variability in healthy people suggesting a marked inter-subject difference in the magnitude of fluctuations in cardiac tone.[3]

Lü Fei *et al* found a statistically significant difference between the minimum heart rate variability in the two groups, whereas there was no difference in the maximum heart rate variability. Because heart rate variability is a physiological perturbation of the sympathetic-parasympathetic axis[4] it is logical to assume that any abnormal autonomic activity would affect equally both the minimum and maximum heart rate variability. Moreover we believe that an integrated 24 hour circadian variation is required to achieve values of sufficient specificity and sensitivity.

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1 Lü Fei, Anderson MH, Katritsis D, Sneddon J, Statters DJ, Malik M, Camm AJ. Decreased heart rate variability in survivors of sudden cardiac death not associated with coronary artery disease. *Br Heart J* 1994; 71:16–21.
2 Norman GR, Streiner DL. PDQ Statistics. BC Decker Inc Philadelphia, 1986.
3 Huikuri HV, Kesslar KM, Terracall E, Castellanos A, Linnaluoto MK, Myerburg RJ. Reproducibility and circadian rhythm of heart rate variability in healthy subjects. *Am J Cardiol* 1990;65:391–3.
4 Malliani A, Lombardi F, Pagani M. Power spectrum analysis of heart rate variability: a tool to explore neural regulatory mechanisms. *Br Heart J* 1994;71:1–3.

This letter was shown to the authors, who reply as follows:

SIR,—We thank Dr Singh and Dr Hart for their interest in our observation that heart rate variability is decreased in non-coronary, high risk patients.[1] However, we believe that their specific comments are mistaken.

The circadian rhythm of heart rate and its variability, like heart rate and heart rate variability themselves, are essentially stable between recordings in both healthy people and survivors of cardiac arrest.[2–4] There is no reason to suspect a difference in the circadian rhythm of heart rate variability in our patients. We confirmed that this was true in our study. It is therefore acceptable to pool the hourly data for statistical analysis. We agree that there are marked inter-subject variations in hourly heart rate variability, but the value of statistics is to test any significant differences based on the individual variations of two groups of pooled data. Bigger *et al* have recently shown that short-term (< 1 h) assessment of heart rate variability is as good at stratifying high risk patients after myocardial infarction as the average values over 24 hours.[5] We also showed that there is a significant change in heart rate variability during the few minutes immediately preceding the onset of spontaneous idiopathic ventricular tachycardia.[6] Obviously these observations do not support the assertion that it is mandatory to use integrated values over 24 hours for the assessment of heart rate variability since, as pointed out in our paper, averaging heart rate variability over 24 hours would mask brief but profound changes in autonomic activity. The significance of the hourly evaluation of heart rate variability was clearly demonstrated in the trends of the circadian distribution of heart rate variability in figure 1. Furthermore, when we used the averaged value of heart rate variability over 24 hours we also showed significantly reduced heart rate variability in the patients studied (table 2).

Dr Singh and Dr Hart assume that the change in the maximum heart rate variability should parallel the change in the minimum value. Our data show that this is not the case, nor would we expect it to be, because factors that depress heart rate variability may only be present intermittently. Intermittent reduction of heart rate variability would extend the extremes of minimum heart rate variability but would not necessarily alter the maximum heart rate variability. The greater reduction in heart rate variability under certain conditions might be of importance in the development of cardiac arrest in these patients. This hypothesis is supported by the observation in an animal experiment that physiological perturbations provoke greater reduction in heart rate variability in dogs susceptible to ventricular fibrillation.[7]

Dr Singh and Dr Hart also suggest that there might have been a difference in physical activities and corresponding autonomic activities between our two groups of subjects. The controls used in our study were age and sex matched and both groups were normally active, as was fully described in our paper. The controls were therefore entirely appropriate.

Finally, we believe that a time series analysis with the auto-regressive or moving-average techniques suggested by Dr Singh and Dr Hart would have been inappropriate for the analysis of our data because the RR interval had already been transformed into the frequency domain during the computation of heart rate variability. We believe that the statistical methods used are appropriate. Short-term inspection of heart rate variability in addition to the overall 24 hour values is necessary under certain circumstances and may provide important information on transient changes of autonomic drive to the heart. This may be particularly important in patients without significant structural heart disease and cardiac dysfunction.

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2 Schmit TF, Engel BT, Blümchen G. Temporal variation of the cardiovascular system. Berlin: Springer-Verlag, 1992.
3 Huikuri HV, Kessler KM, Terracall E, Castellanos A, Linnaluoto MK, Myerburg RJ. Reproducibility and circadian rhythm of heart rate variability in healthy subjects. *Am J Cardiol* 1990;65:391–3.
4 Huikuri HV, Linnaluoto MK, Seppänen T, Airaksinen KE, Kessler KM, Takkunen JT, Myerburg RJ. Circadian rhythm of heart rate variability in survivors of cardiac arrest. *Am J Cardiol* 1992;70:610–5.
5 Bigger JT Jr, Fleiss JL, Rolnitzky LM, Steinman RC. The ability of several short-term measures of RR variability to predict mortality after myocardial infarction. *Circulation* 1993;88:927–34.
6 Lü Fei, Statters DJ, Malik M, Camm AJ. Changing in autonomic influence on the heart immediately before the onset of spontaneous idiopathic ventricular tachycardia [abstr]. *J Am Coll Cardiol* 1994;23(suppl): 322A.
7 Billman GE, Hoskins RS. Time-series analysis of heart rate variability during submaximal exercise. Evidence for reduced cardiac vagal tone in animals susceptible to ventricular fibrillation. *Circulation* 1989;80:146–57.