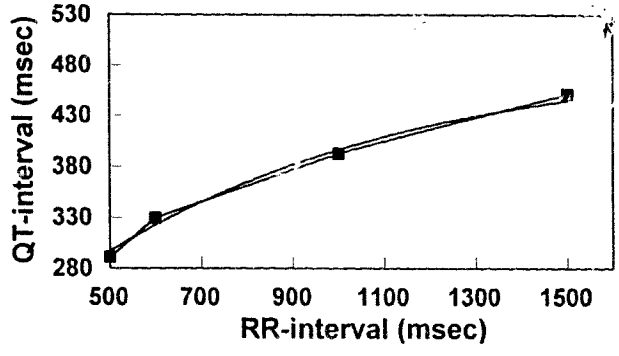
LETTERS TO THE EDITOR

Relation Between QT and RR Intervals

Karjalainen et al. (1) showed that a single linear equation is inadequate to represent the QT-RR relation over a wide range of RR intervals in healthy young men. They developed a nomogram for measured QT intervals to obtain a heart rate-adjusted QT value, using three linear regression equations for three ranges of RR intervals (<600, 600 to 1,000 and >1,000 ms). They compared their analysis with three other formulas but not with the exponential formula, which should have been considered, because their linear equations had decreasing slopes with increasing RR values. In Figure 1 (shown here), we reproduced the three regression lines as given in their Figure 3 and superimposed a single exponential curve defined by the equation $QT = 491 - 398 \times \exp(-RR/697)$. We derived this equation by requiring the exponential curve to go through three selected points on their regression lines. Nonlinear regression analysis on their raw data might yield a slightly different exponential curve. As can be seen from Figure 1, the exponential curve closely approximates the entire range of data, thus virtually eliminating the need for three different equations. The curve-fitting procedure presented by Karjalainen et al. (1) may still be essentially valid because it amounts to approximating a nonlinear relation with a piecewise linear function. However, the exponential equation may be more physiologic in this context because it provides an upper limit to the value of the QT interval for very long RR intervals (2) (see also Editorial Comment by Franz [3]). It is well known that many natural phenomena are described by exponential equations. The piecewise linear approximation with a total of six parameters, compared with three for the exponential function, violates the principle of parsimony generally observed for empiric curve fitting (2).

There are theoretic limitations common to all population-derived multiparameter formulas when they are applied to correct a measured QT interval from an individual patient. The best fitting formula can reliably estimate how much the measured QT interval deviates from the normal population value at the prevailing heart rate of the patient. However, there is no existing method to estimate the patient's QT interval at a different heart rate (e.g., 60 beats/min) without making the arbitrary assumption that the intrinsic QT-RR relation for that patient is exactly parallel to the population curve. Such an assumption, for example, ignores the possibility of reverse use dependency of class III antiarrhythmic drug action (3). Otherwise, the problem is the mathematical equivalent of one equation and multiple unknowns. The nomogram presented by Karjalainen et al. (1) is subject to this insurmountable limitation.

Figure 1. The lines connecting the **square symbols** represent the three regression lines proposed by Karjalainen et al. (1). The **solid smooth curve** represents a single exponential equation derived to closely approximate all three lines.



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Correcting the QT Interval: Is It Relevant?

I read with interest the novel approach by Karjalainen et al. (1) to correct the QT interval on the basis of the prevailing heart rate. From the results of their study it could be seen that the mean-squared residual values for the nomogram correction had increased in the middle-aged subjects compared with those in the younger, healthy male group (on the basis of whom the nomogram was derived). This in itself implies the relative inadequacy of the nomogram for the middle-aged subjects. A nomogram would be acceptable to predict a change in a dependent variable that has a direct and fixed relation with only one other independent variable. However, the QT interval is a dynamic interval that is affected by multiple factors, such as exercise, catecholamine levels, diurnal variations, electrolyte levels and autonomic tone, in addition to heart rate (2). It thus appears rational to infer that the QT interval would respond differently in different hemodynamic settings, making a nomogram inapplicable for correcting the QT interval in different disease states.

The authors also fail to mention the clinical state of the subjects when the QT interval was recorded at high heart rates. An important physiologic response to take into consideration is the QT hysteresis effect (3) that results from the exercise-recovery cycles accompanying daily routine activities and which itself could interfere with correction of the QT interval. It is important that the correction formula be limited to the steady state because there is a risk of overcorrection or undercorrection during any physiologic or pharmacologic maneuvers.

In view of these multiple influences on the QT interval, it appears unlikely that any linear correction formula or nomogram could appropriately correct the QT interval. Moreover, on 24-h ambulatory QT monitoring, the QT correction formula derived by linear regression

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over 1 h, using a beat-to-beat QT and RR interval measurement, may not apply to the next hour in the same patient. This may occur because RR-QT data collected during the course of the day tend to show considerable scatter because of the normal fluctuations in autonomic tone. With this in mind, one really wonders whether correcting the QT interval makes any sense at all?

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Reply

We thank Sarma et al. and J. Singh for their comments on our recent publication in the Journal (1) The inaccuracy of Bazett's method for adjusting QT intervals has caused bias in research and confusion in clinical practice. The popularity of the Bazett equation is based on its simplicity, not on its fit. The newer improved but complex methods have largely been ignored. Our goal was to create a simple and accurate method to compare QT intervals of *rest electrocardiograms* (ECGs) without violating the electrophysiologic principles derived from action potential studies (2).

Sarma et al. derived an exponential equation using our data. Their equation produces an average mean-squared residual value of 304, whereas our nomogram method gives the value of 291 in young men (Table 3 [1]). Notwithstanding the possible advantages at very low heart rates, the use of an exponential equation is problematic in clinical practice, which is why we avoided presenting one. The major advantage of the nomogram method is that it is empiric and has no limiting preassumptions. The disadvantage of all regression equations is that the same rule is applied over the entire range of heart rates.

As pointed out by J. Singh, the nomogram works at steady state only. This was ensured in our study by recording ECGs at rest, as stated in the report's title. Estimating the patient's QT interval at a different heart rate, a question raised by Sarma et al., is really another matter, as shown in Figure 7 in our study (1).

Sarma et al. write that there is an insurmountable limitation to our method for estimating the QT interval in patients using class III antiarrhythmic drugs, whereas J. Singh reminds us that the nomogram presented may be inapplicable in disease states. These are important issues, similarly applicable to all equations for adjusting QT intervals. If the goal is to evaluate the effect of antiarrhythmic drugs or a disease process on the QT interval, then the Holter method should be chosen (3,4). In the Holter method the need for heart rate adjustment is avoided by measuring the QT intervals at the same spontaneous heart rates before and after intervention.

J. Singh asks whether there is any sense at all in correcting the QT interval. Because there is no such thing as a single correct QT interval, we preferred the term *adjusted QT interval*. Although the dynamic changes in the QT interval and the dispersion of repolarization may be of greater importance in arrhythmogenesis, in clinical practice one should be able to evaluate the QT interval in the rest ECG reliably. Moreover, the QT interval in the rest ECG is the key to understanding QT dynamics. When the most reliable QT interval-adjusting tools for rest ECGs for different populations of patients under medication are needed, they should be constructed for the particular population using the principle presented, for example. When the effects of medication or the disease process on the QT interval in an individual patient have to be evaluated, we recommend the Holter method (3).

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Atrial Function Can Only Be Assessed by Combined Use of Volume- and Pressure-Assessing Noninvasive Methods

In the recent study of Manning et al. (1) a new index for assessing the atrial contribution to diastolic performance was introduced. Using Newton's second law of motion and variables derived from two-dimensional imaging and Doppler echocardiography, the authors attempted to introduce a more accurate mode of assessing atrial function in 29 patients after elective cardioversion for atrial fibrillation. When Newton's law is replaced by echocardiographic variables, the "atrial ejection force" is proportional to peak A velocity squared and varies directly with mitral orifice area. Although the atrial ejection force was found to be significantly reduced in the patients compared with a small group of normal control subjects, this new index does not represent an assessment of "atrial function" or "atrial contribution" in these patients with coronary and hypertensive heart disease because there are several problems with the interpretation of this major finding by the authors.

Manning et al. mention that, according to data of Choong et al. (2), "peak A wave velocity is over a physiologic range relatively independent of ventricular preload." However, they do not emphasize another important finding, namely that in patients with clearly abnormal diastolic function and elevated ventricular filling pressures, peak A velocity is predominantly, if not exclusively, dependent on the degree of elevation of end-diastolic pressure. Obviously, the patients in the Manning et al. study could be expected to have at least a moderate