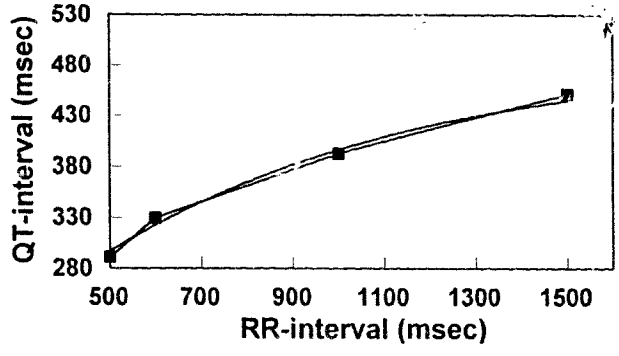
LETTERS TO THE EDITOR

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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