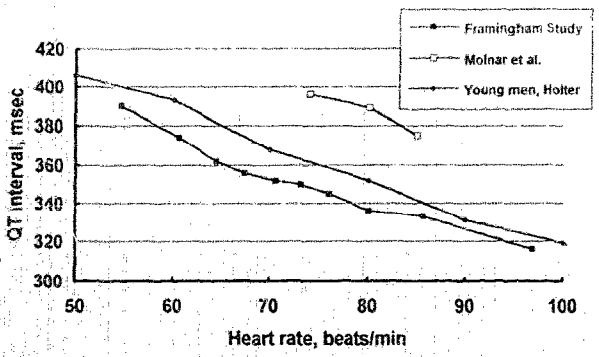

Figure 1. Measured QT intervals at different heart rate levels in the study of Molnar et al., the Framingham study and a Holter study of young healthy men.

Framingham study (one QT measurement/subject [all men], manual measurement of the longest QT interval on the 12-lead rest electrocardiogram, paper speed 25 mm/s) and in the study of Molnar et al. (measured from their Fig. 3 for the time between 11 AM and 8 PM, when all subjects were awake). The 21 subjects of Molnar et al. also included 10 women and were somewhat older (mean 57 years, range 36 to 76) than those in the Framingham Study (mean 44 years, range 28 to 62). However, according to the data of Rautanarju et al. (3), this age and gender difference would be responsible for only ~5 ms of the difference in measured QT intervals. To exclude the role of the ambulatory situation in QT measurement, we also included in Figure 1 our QT interval data for 100 young healthy men (18 to 30 years old) measured at stable heart rates 50, 60, 70, 80, 90, 100, 110 and 120 beats/min from 24-h Holter recordings (4). These QT intervals are 30- to 40-ms shorter at respective heart rates than those reported by Molnar et al. (the effect of age and gender differences is expected to be <5 ms [3]). Thus, the reason for the clear differences between these three studies must lie in the methodology of QT measurement. If Molnar et al. consider the manual QT measurements of the Framingham study incorrect, it is surprising that they use the formula derived from the Framingham study data in the heart rate correction of their QT intervals, without discussing the correctness of this procedure.

We think that the data presented by Molnar et al. emphasize the importance of publishing the QT interval measurement algorithms used in the commercial Holter analysis systems. Only then will it be possible to try to standardize the methodology of the automatic QT interval measurement and obtain QT data that can be compared from one study to another.

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References

1. Molnar J, Zhang F, Weiss J, Ehlert FA, Rosenthal JE. Diurnal pattern of QTc interval: how long is prolonged? Possible relation to circadian triggers of cardiovascular events. J Am Coll Cardiol 1996;27:76–83.
2. Sagie A, Larson MG, Goldberg RJ, Bengtson JR, Levy D. An improved method for adjusting the QT interval for heart rate (the Framingham Heart Study). Am J Cardiol 1992;70:797–801.
3. Rautaharju PM, Zhou SH, Wong S, et al. Sex difference in the evolution of the electrocardiographic QT interval with age. Can J Cardiol 1992;8:690–5.
4. Viitasalo M, Karjalainen J. QT intervals at heart rates from 50 to 120 beats per minute during 24-hour electrocardiographic recordings in 100 healthy men: effects of atenolol. Circulation 1992;86:1439–42.

Reply

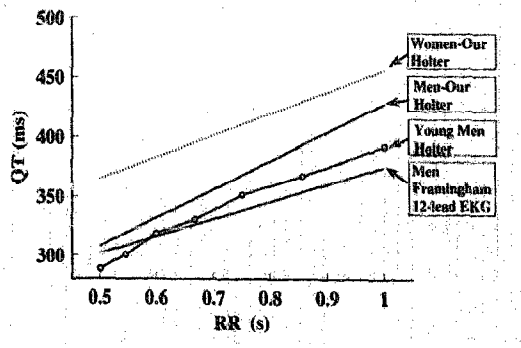
We thank Mäntysaari et al. for their interest in our report and for their comments regarding the comparability of our data with those published elsewhere. We share their concern about the lack of standardized methodology for QT interval measurement.

The values for each of the curves in their Figure 1 were obtained using different methods: For the curve showing the Framingham data (1), the mean QT intervals were calculated for gender-specific deciles of RR values. For the curve showing data from the study by Viitasalo and Karjalainen (2), the QT intervals were collected at stable heart rates. Regarding our study (3), Mäntysaari et al. graphically interpreted hourly mean RR and QT interval data from our Figure 3. We have two major concerns about this data interpretation:

1. Data points from our study represent something different than those from the other two studies, in which QT values were measured at specific heart rates. Our data, in contrast, represent hourly average QT and RR intervals, and, as such, there is a wide range of values underlying them.
2. The relation between heart rate and RR interval is not linear. Therefore, average RR intervals, as reported in our Figure 3, cannot be readily converted into average heart rate, as the Mäntysaari et al. have done with our data. For example, for two QT intervals measured at heart rates of 60 beats/min (RR 1 s) and 100 beats/min (RR 0.6 s), the average QT interval would be plotted at the average heart rate of 80 beats/min. However, if the average heart rate is determined from RR intervals that have been converted to heart rate, the resulting rate is 75 beats/min [(1 s + 0.6 s)/2 = 0.8 s = 75 beats/min]. Thus, details of the method by which data are analyzed can produce differing results, thereby shifting the position of the QT interval versus RR curve.

We reanalyzed the data cited in the letter of Mäntysaari et al. using, as much as possible, comparable analytic techniques for each of the three studies. We assessed the QT intervals from our study (3) as a function of the RR interval and fitted them using the Framingham formula. The regression lines, as well as the regression line for men from the Framingham study (1) and the actual values of "Young men, Holter" of Viitasalo et al. (2) are shown in our Figure 1. The heart rate data of

Figure 1. QT versus RR relationship from three studies using Holter monitoring and 12-lead electrocardiogram (see text for details).



Viitasalo and Karjalainen could be converted to RR values because they were not averaged. It is apparent that in our study, the QT interval at each RR value for women compared with that for men was longer than previously reported (12 ms, QT interval obtained from a single 12-lead electrocardiogram at rest [1]). The explanation for this discrepancy may at least in part be that in our 24-h Holter study, women displayed substantially greater nighttime QT prolongation than men. In men there is good agreement between studies at short cycle lengths: Between the two Holter studies, differences are <20 ms (range 13 to 18) at an RR interval of 0.50 to 0.75 s. At lower heart rates, the differences are larger, probably because only our data include values obtained during sleeping hours. Considering that 1) our patients were older, and 2) the range of individual QT measurements at a given heart rate is typically wide, our results differ less markedly from those obtained in other studies than stated in the letter of Mäntysaari et al.

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References

1. Sagie A, Larson MG, Goldberg RJ, Bengston JR, Levy D. An improved method for adjusting the QT interval for heart rate (the Framingham Heart Study). Am J Cardiol 1992;70:797–801.
2. Viitasalo M, Karjalainen J. QT intervals at heart rates from 50 to 120 beats per minute during 24-hour electrocardiographic recordings in 100 healthy men: effects of atenolol. Circulation 1992;86:1439–42.
3. Molnar J, Zhang F, Weiss J, Ehlert FA, Rosenthal JE. Diurnal pattern of QTc interval: how long is prolonged? Possible relation to circadian triggers of cardiovascular events. J Am Coll Cardiol 1996;27:76–83.